The McGraw-Hill Companies

Human Anatomy and Physiology

(With Health Education)

About the Author

Padma B Sanghani has been supervising an EMG centre in Gujarat for the past 19 years. She obtained MBBS degree from Gujarat University and was the recipient of Rai Bahadur Dr J P Mody and Smt. Mody Gold Medal in Forensic Medicine. She also obtained the Smt. Shantaben B Desai Gold Medal and the President of India's Silver Medal for securing the highest marks among female candidates in Gujarat University in 1970–71. She then went on to obtain MD degree in General Medicine and Therapeutics in 1975 and underwent training in Electrophysiology Studies at Jaslok Hospital. Dr Sanghani's other merit awards include Dr M S Kanvinde Gold Medal in second-year MBBS (Pathology) in the year 1969; and Smt. Chimanlal Lalbhai Gold Medal (Surgery) in the year 1970.

She joined V S General Hospital affiliated to Smt NHL Municipal Medical College, Ahmedabad, and from 1970 to 1976 held various posts like Senior Registrar and Assistant Professor in Neurology. She has also delivered guest lectures at Gujarat University, NIRMA University and other institutions and is Associate Professor of Biomedical Studies at U V Patel College of Engineering.

Dr Sanghani's research work includes evaluation of the drug *Nitrong* in Angina Pectoris under the sponsorship of M/s Sarabhai Chemicals in collaboration with SQUIBB, USA; and evaluation of muscle relaxants in tetanus.

Her subject of special interest is Neurology and she has published an article on Unusual Cause of Sub-Arachnoids Haemorrhage, and Bilateral Internal Carotid Occlusion.

Dr Sanghani is a life member of Medical Association Kalol (a branch of Gujarat Medical Association), Association of Physicians of Gujarat, Association of Physicians of India, Biomedical Engineering, Neurological Society of India, and Neuroscientists Association of Gujarat.

Dr Sanghani's family includes her husband, Dr Bakul Sanghani, her daughter, son-in-law and two granddaughters.

The McGraw-Hill Companies

Human Anatomy and Physiology

(With Health Education)

Padma B Sanghani
Practicing Neuro-Physiologist
and
Visiting Professor
U V Patel College
Ganpat University
Mehsana, Gujarat

Tata McGraw Hill Education Private Limited
NEW DELHI

McGraw-Hill Offices
New Delhi New York St Louis San Francisco Auckland Bogotá Caracas
Kuala Lumpur Lisbon London Madrid Mexico City Milan Montreal
San Juan Santiago Singapore Sydney Tokyo Toronto

The McGraw-Hill Companies

Tata McGraw-Hill

Published by the Tata McGraw Hill Education Private Limited,
7 West Patel Nagar, New Delhi 110 008.

Human Anatomy and Physiology (With Health Education)

This edition can be exported from India only by the publishers,
Tata McGraw Hill Education Private Limited

ISBN-13: 978-0-07-107773-6
ISBN-10: 0-07-107773-1

Vice President and Managing Director—McGraw-Hill Education, Asia-Pacific Region: *Ajay Shukla*
Head—Higher Education Publishing and Marketing: *Vibha Mahajan*
Publishing Manager (SEM & Tech. Ed.): *Shalini Jha*
Editorial Executive: *Smruti Snigdha*
Development Editor: *Renu Upadhyay*
Executive—Editorial Services: *Sohini Mukherjee*
Asst. Manager—Production: *Anjali Razdan*

Marketing Manager—Higher Education: *Vijay S Jagannathan*
Product Specialist: *Sachin Tripathi*

General Manager—Production: *Rajender P Ghansela*
Assistant General Manager—Production: *B L Dogra*

Typeset at The Composers, 260, C.A. Apt., Paschim Vihar, New Delhi 110 063 and printed at
AP Offset Pvt. Ltd., 25/487, Zulfe Bengal, Dilshad Garden, New Delhi-110095

Cover Design: Meenu Raghav, Graphic Designer, TMH

Cover Printer: AP Offset

RZZCRRQWDQRYL

The McGraw-Hill Companies

Contents

The McGraw·Hill Companies

Preface

Overview

This book will primarily cater to students of pharmacy who need to have fundamental knowledge of *Human Anatomy and Physiology*. It will also be equally useful to the students graduating in physiotherapy, nursing, dentistry and biomedical fields.

In my seven years of teaching experience, I observed that students of pharmacy and allied health courses had a difficult time understanding the complex language and reading big, bulky textbooks of medicine for their limited syllabus. They required a book that was simple and easy to follow. This encouraged me to write a book for pharmacy students. The present text is designed in view of the pharmacy syllabi of Indian universities.

Salient Features

This book deals with the systems of the body with reference to anatomy and physiology and I have attempted to achieve maximum coverage in the simplest way. Given below are some important features of the book:

- Exactly as per undergraduate pharmacology standard curricula, prescribed by PCI guidelines
- Easy-to-follow, step-wise, self-explanatory and student-friendly approach
- Complete coverage to all important topics like Cell Structure and Function, Tissues, Major Organ Systems, Physiology of Aging
- Explanation of pathophysiology of each disease from its genesis
- Well-labeled 800 illustrations
- 250 chapter-end review questions

Chapter Organisation

The first four chapters describe the body and its constituents, making it possible to understand the functioning of the body. Along with anatomy and physiology, diseases and disorders have been described with their pathophysiology. Chapters on the nervous system, endocrine system, cardiovascular system, especially cardiac arrhythmias and investigations in cardiology, have received elaborate coverage. This would help students understand how and where drugs act. Immunology, Physiology of aging and Communicable diseases have also received extensive coverage. Chapters on the Lymphatic system, Integumentary system, Communicable diseases and health education enhance the knowledge of students. Ion channels and transmission of impulses at various levels receive a good amount of importance.

Each chapter carries a brief outline of the topics discussed. Then there is a detailed description of the anatomy of the particular organ system along with its functions followed by the physiology, using simple, understandable language to make learning easy.

All the chapters are replete with tables to highlight certain aspects, show differences and chiefly to make things easy for the students.

Online Learning Centre

The associated website for this book is available at http://www.mhhe.com/sanghani/hap and contains an exhaustive store of Review Questions, Sample Chapters, PowerPoint presentations and more.

Acknowledgements

This book would not have been possible without the guidance of many people. The suggestions received from professors of pharmacy colleges in Gujarat helped make this book complete with full coverage of all necessary topics. I am indebted to them.

I would also like to mention the contributions of certain reviewers in this regard whose names are given below:

Niyati Acharya	Institute of Pharmacy, Nirma University, Ahmedabad, Gujarat
Vandit Trivedi	K B Institute of Pharmaceutical Education and Research, Gandhinagar, Gujarat
R Sheela Devi	Dr ALM PG Institute of Basic Medical Sciences, University of Madras, Chennai
David Banji	Nalanda College of Pharmacy, Nalgonda, Andhra Pradesh
S Vasudeva Murthy	Jayamukhi College of Pharmacy, Warangal, Andhra Pradesh
Meenu Singh	CMR College of Pharmacy, Hyderabad, Andhra Pradesh
Satish B Bhise	Sinhagad Institute of Pharmaceutical Sciences, Lonavala, Maharashtra
Umakant Bajaj	Ram-Eesh College of Pharmacy, Uttar Pradesh
Guatam Chatterjee	Bengal School of Technology Chinsurah, West Bengal
M Ramanathan	PSG College of Pharmacy, Coimabatore, Tamil Nadu
Bhaskar Mahadev Patil	Rajgad Dyanpeeth College of Pharmacy, Pune, Maharashtra

A special note of thanks is due to Mr Sameer Patel, Asst. Prof. in Pharmacy, Kalol Institute of Pharmacy; Mr Sanjeev Acharya, Assoc. Prof. of Pharmacognosy, Nirma University; and Mr Rameshwar Patel, Asst. Prof. in Pharmacy, Ganpat University, for their valuable suggestions.

Finally, my sincere thanks to the staff of Tata McGraw Hill for their help and guidance during the development of the book not only for the students but also for the teachers.

Padma Sanghani

Publisher's Note

Do you have a feature request? A suggestion? We are always open to new ideas (the best ideas come from you!). You may send your comments to *tmhsciencemathsfeedback@gmail.com* (kindly mention the title and author name in the subject line).

Chapter 1

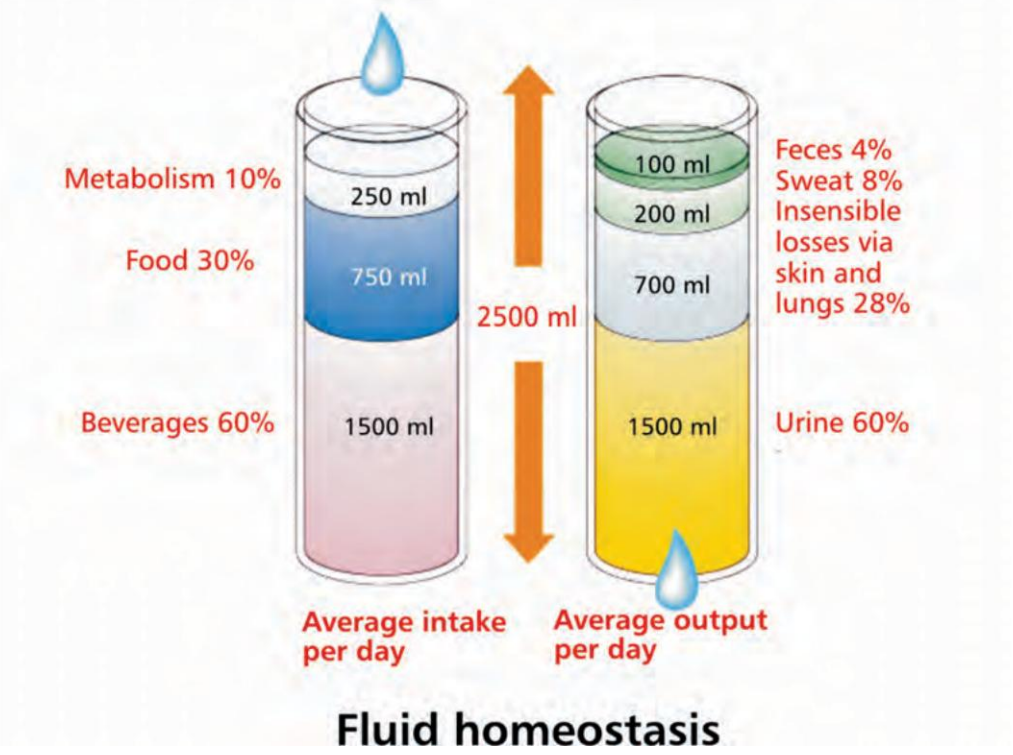


Fig. 1.5

Chapter 2

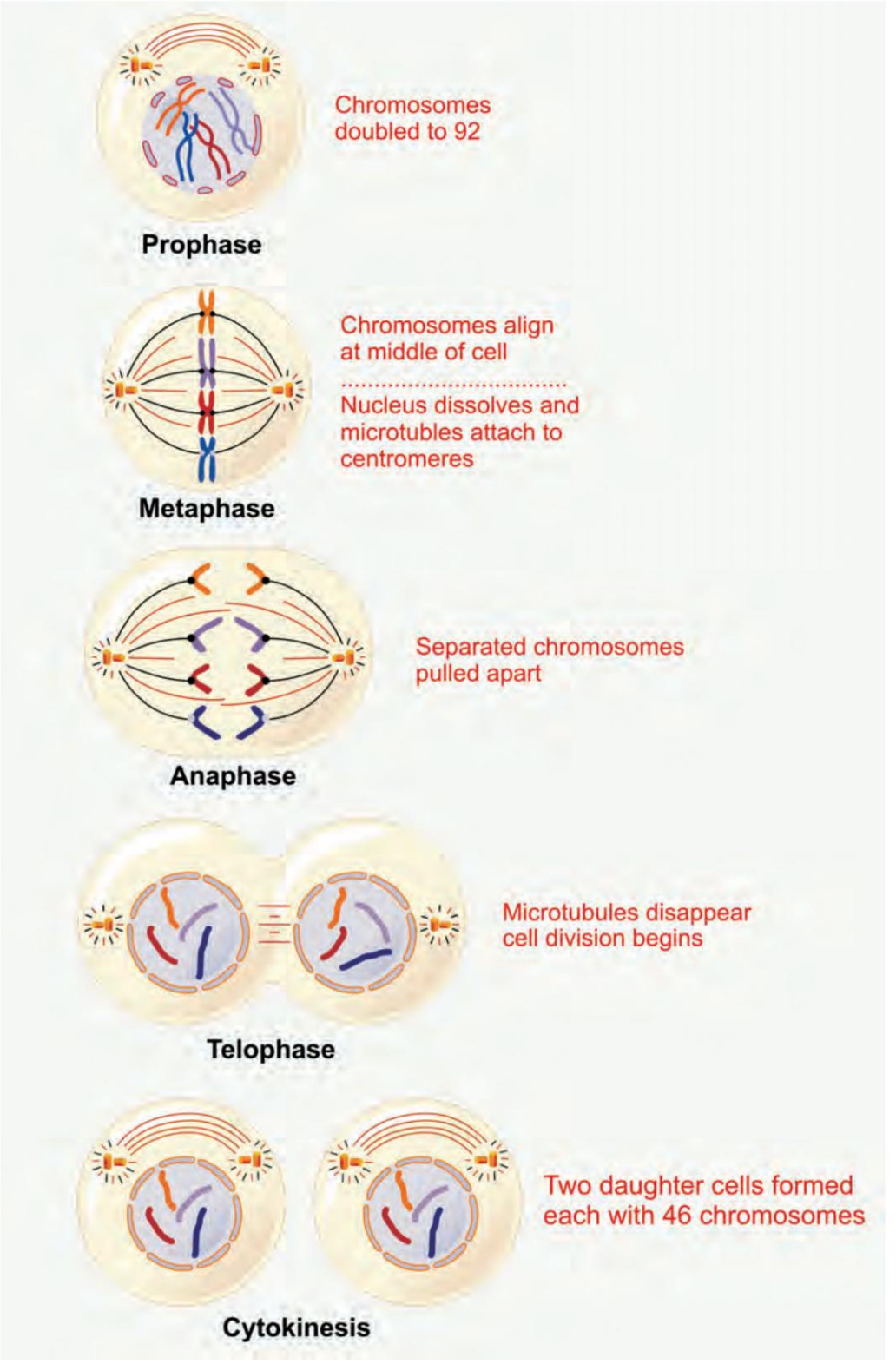


Fig. 2.25

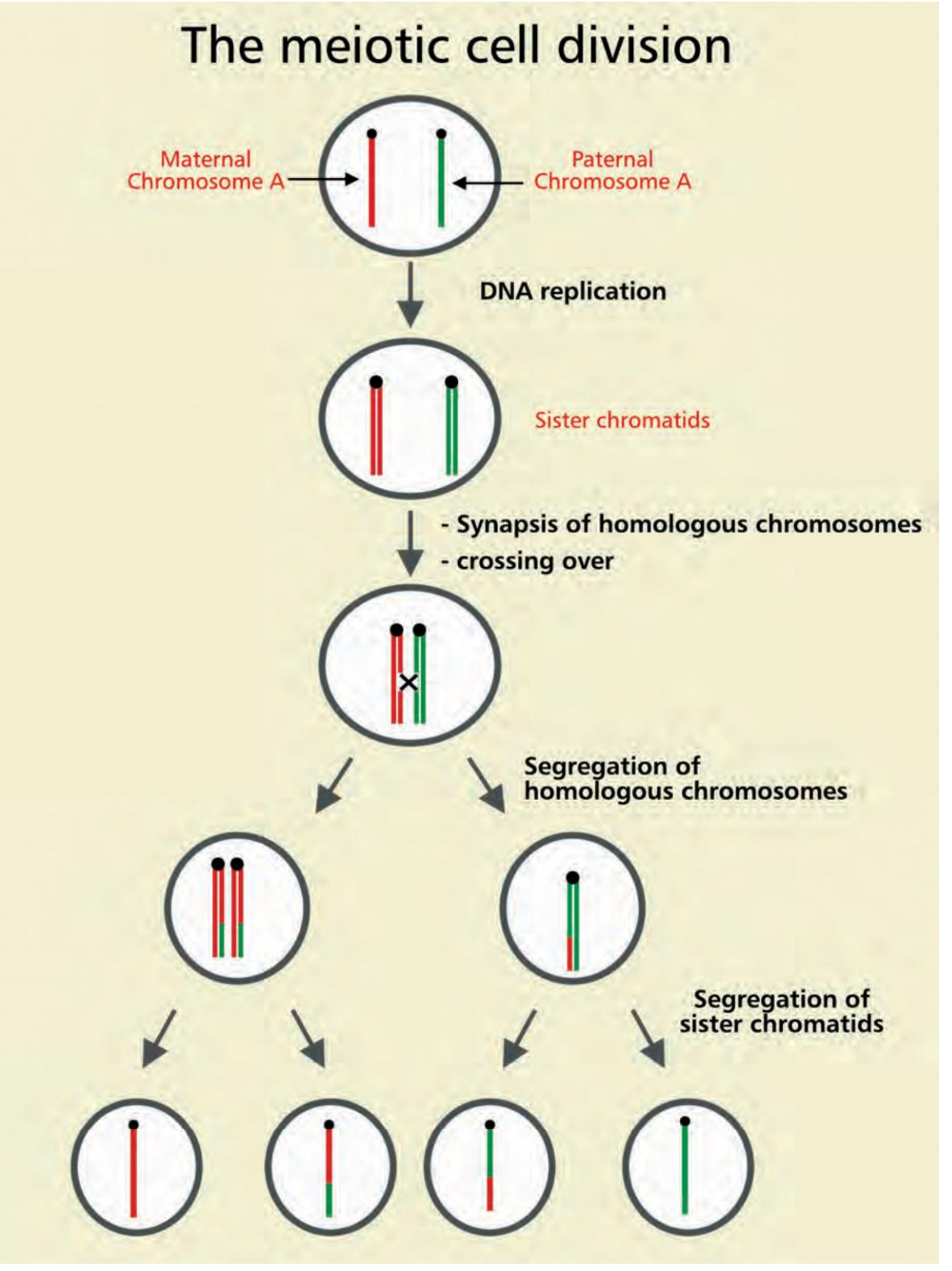

The meiotic cell division
Maternal Chromosome A
Paternal Chromosome A
DNA replication
Sister chromatids
- Synapsis of homologous chromosomes
- crossing over
Segregation of homologous chromosomes
Segregation of sister chromatids

Fig. 2.26

Chapter 4

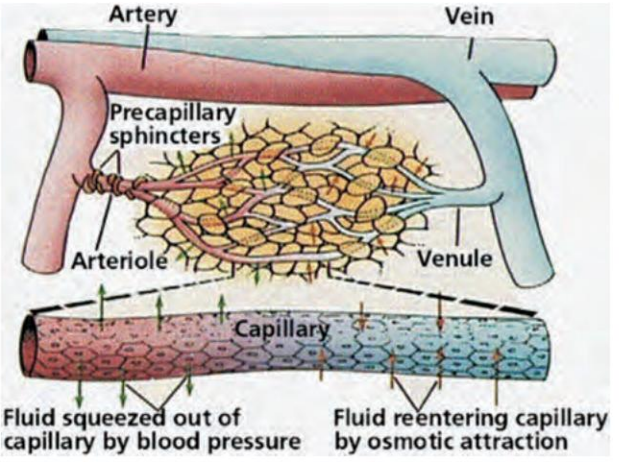


Fig. 4.2

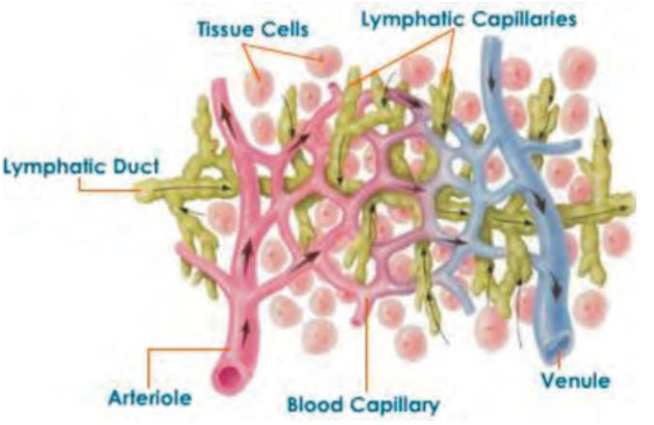


Fig. 4.3

Chapter 5 Skelatal System

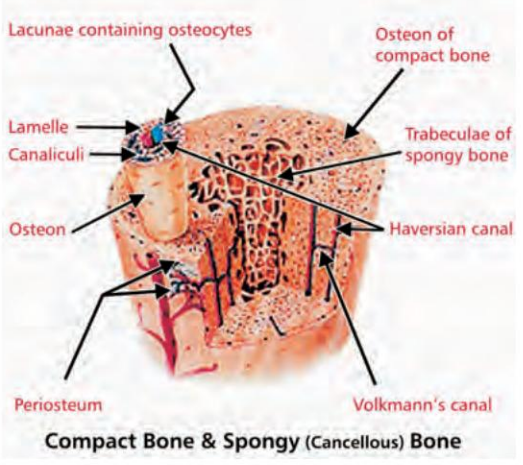


Fig. 5.3

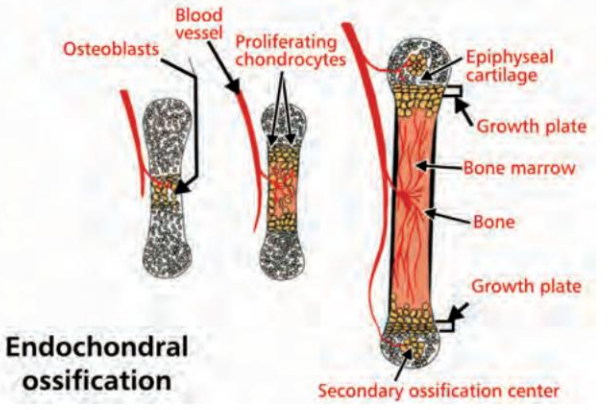


Fig. 5.4

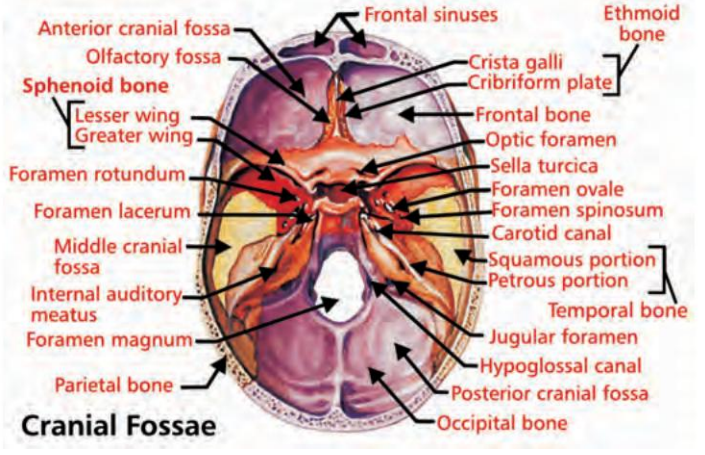


Fig. 5.9

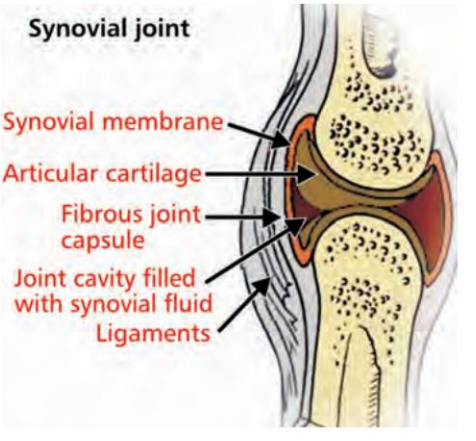


Fig. 5.26

Chapter 6 Muscular System

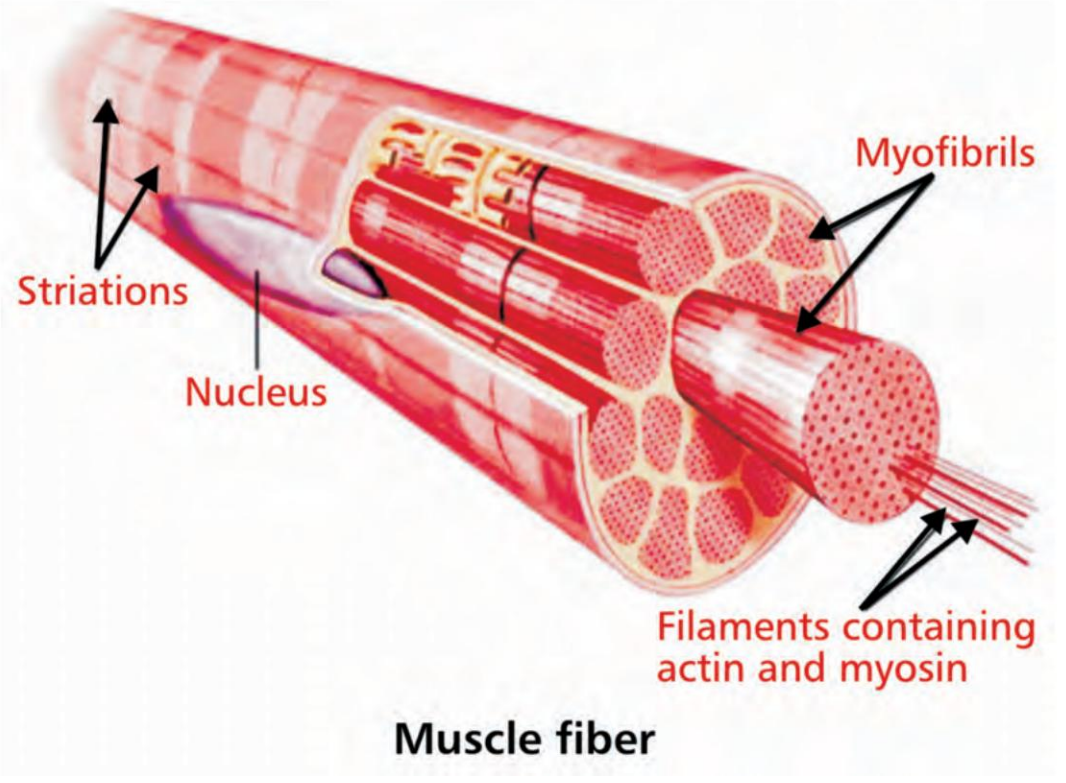
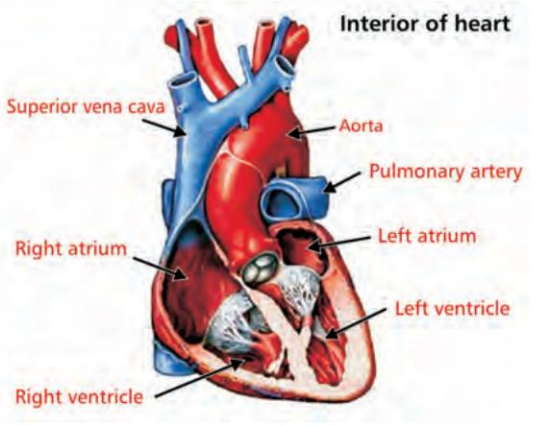


Fig. 6.2

Chapter 7 Cardiovascular System



Heart and its chambers

Fig. 7.2

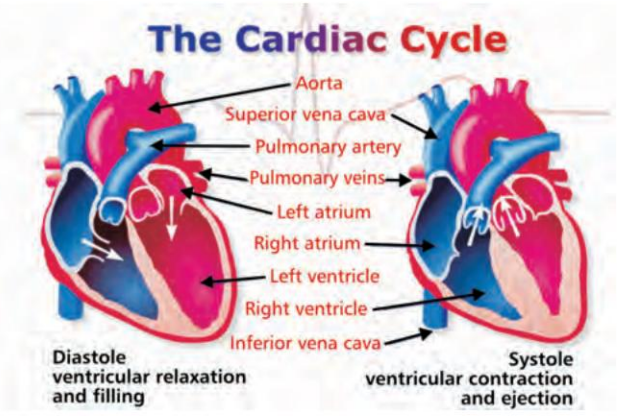
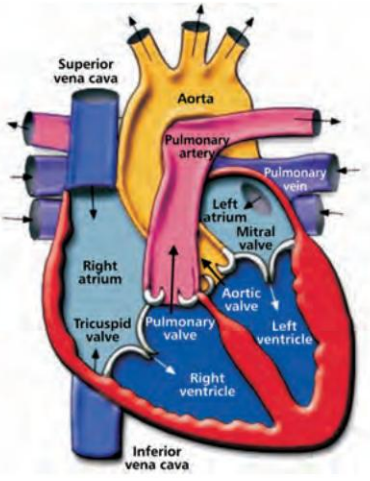


Fig. 7.15



Valves of the heart

Fig. 7.4

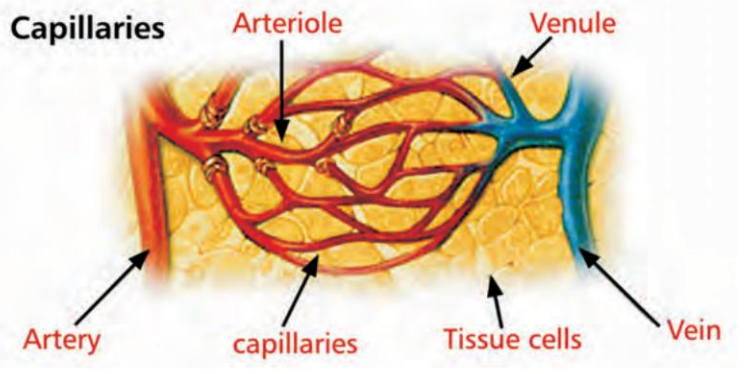
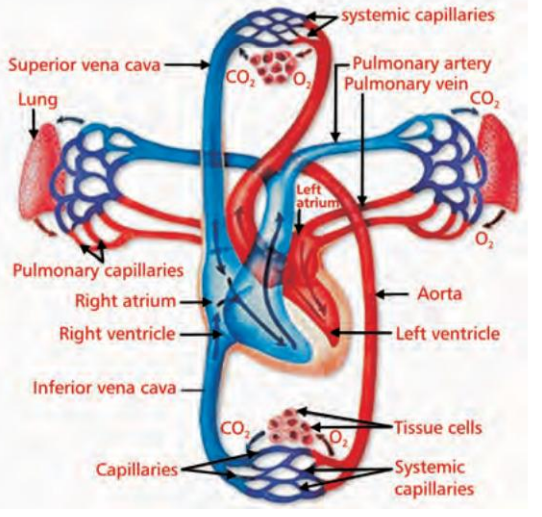


Fig. 7.8



Pulmonary circulation

Fig. 7.32

Chapter 8 Respiratory System

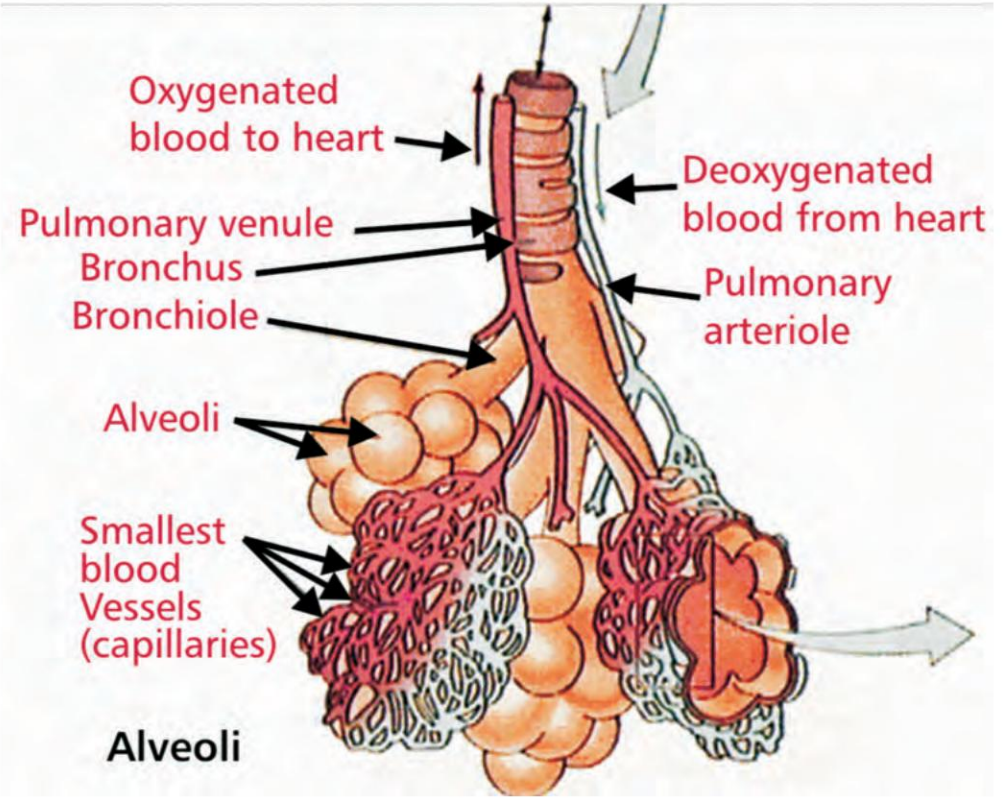


Fig. 8.9

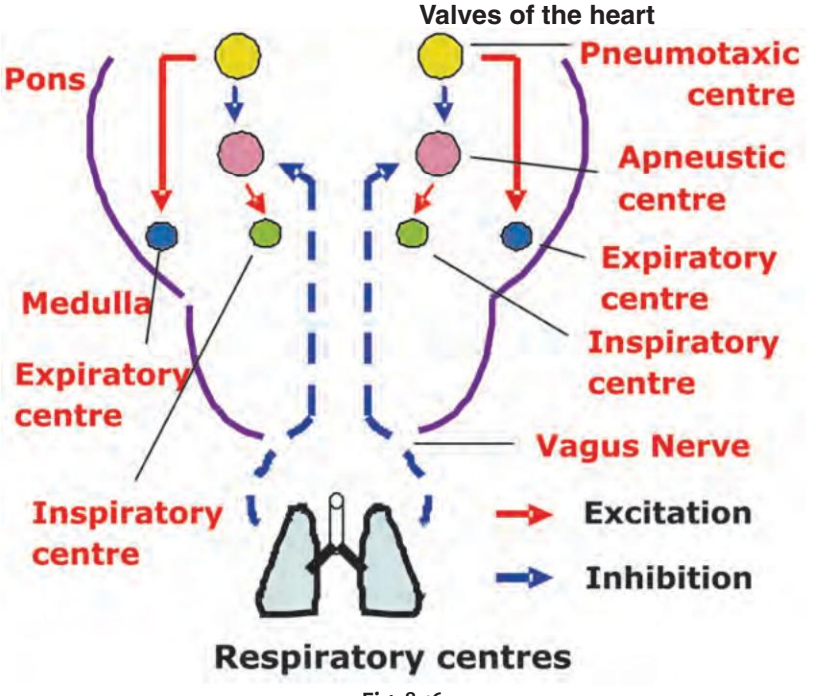
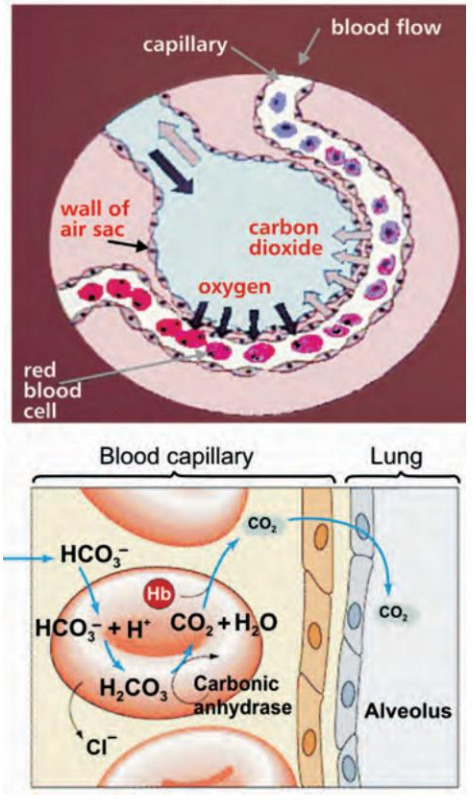
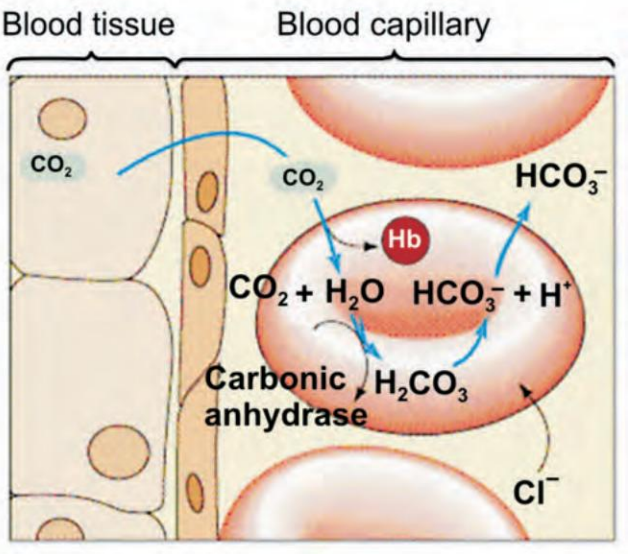


Fig. 8.16

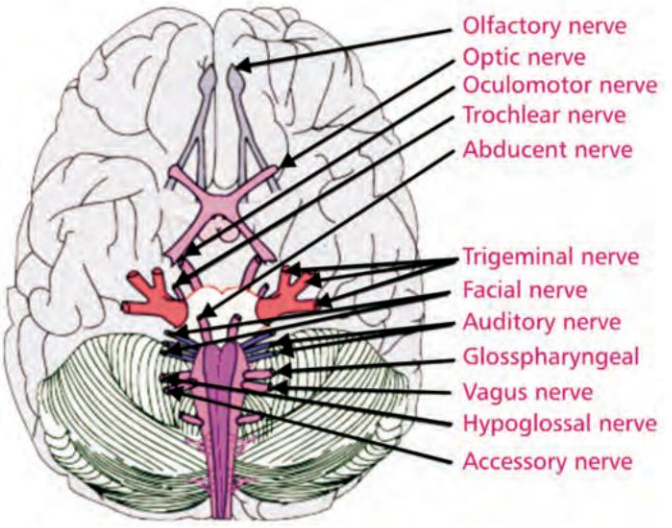


External respiration
Fig. 8.18



Internal respiration
Fig. 8.19

Chapter 10 Nervous System



Origin of cranial nerves

Fig. 10.3

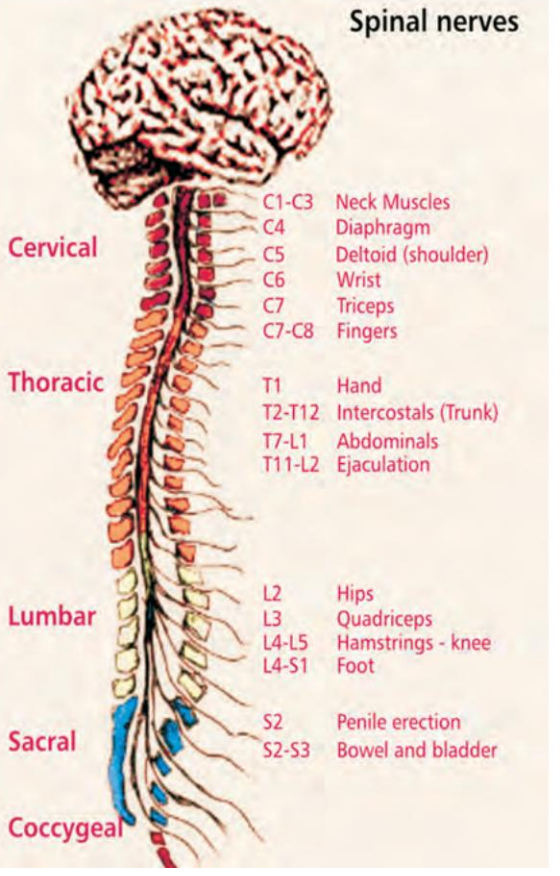


Fig. 10.4

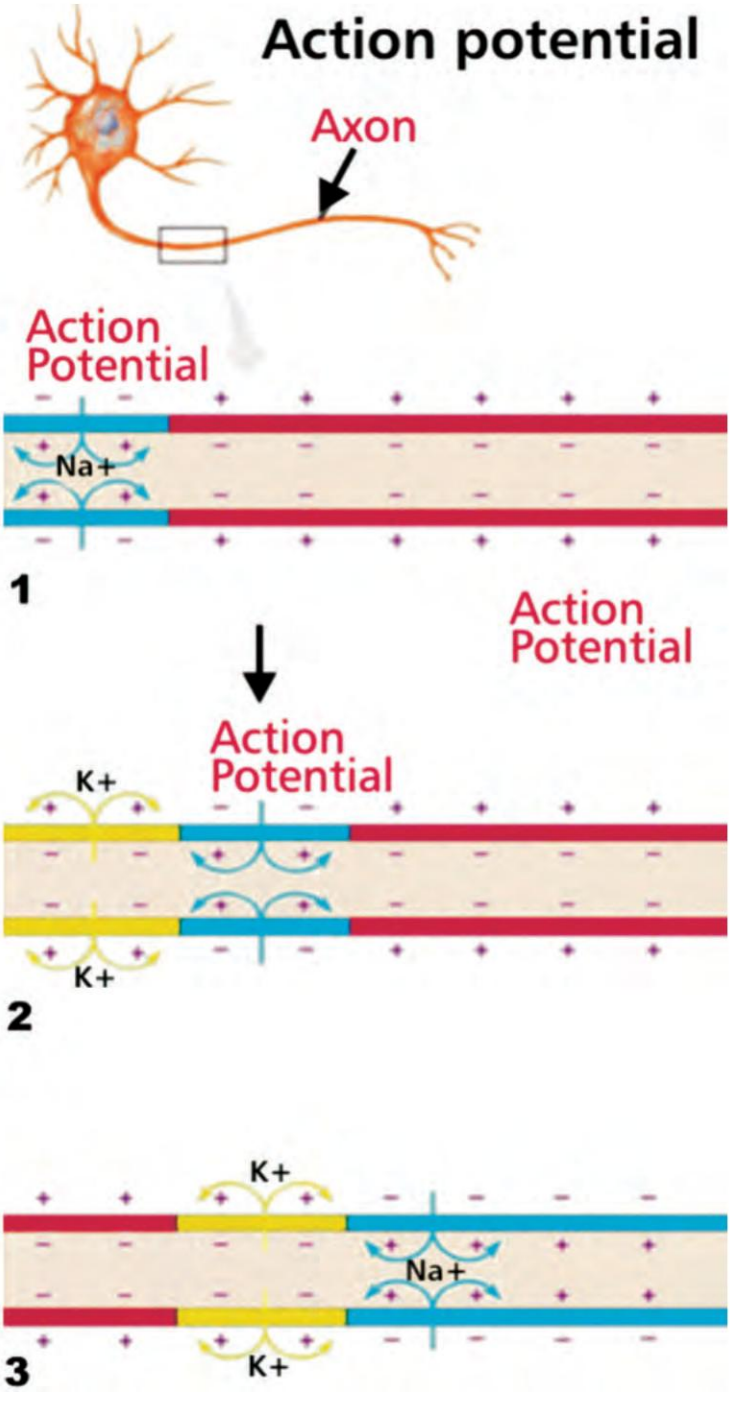

Action potential
Axon
Action Potential
Na+
1
Action Potential
Action Potential
K+
K+
2
K+
Na+
K+
3

Fig. 10.21

Chapter 11 Special Senses

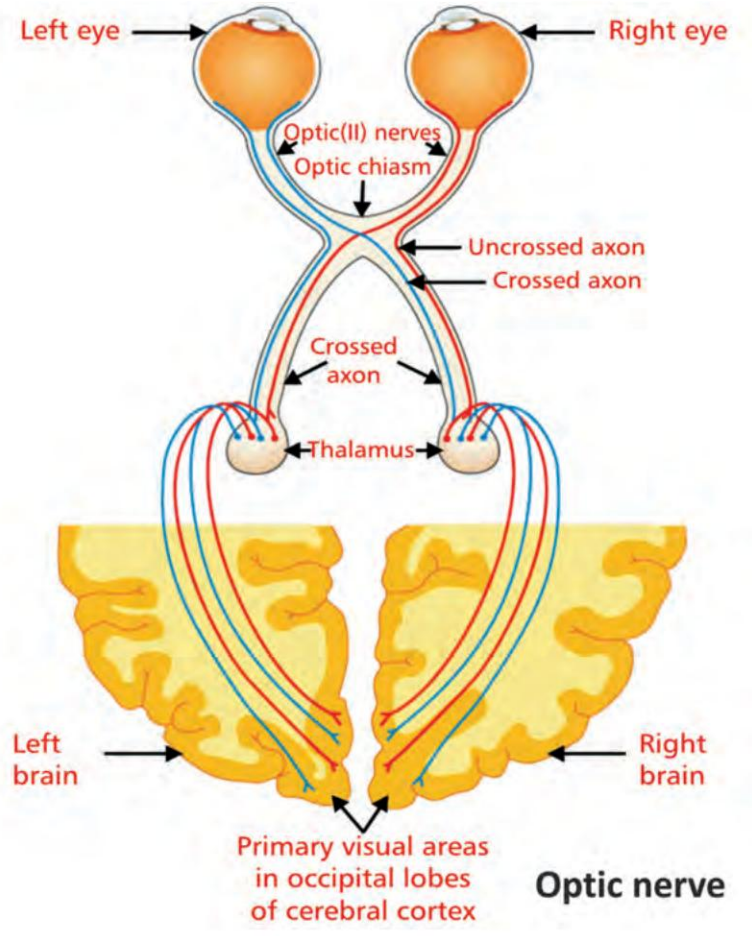


Fig. 11.5

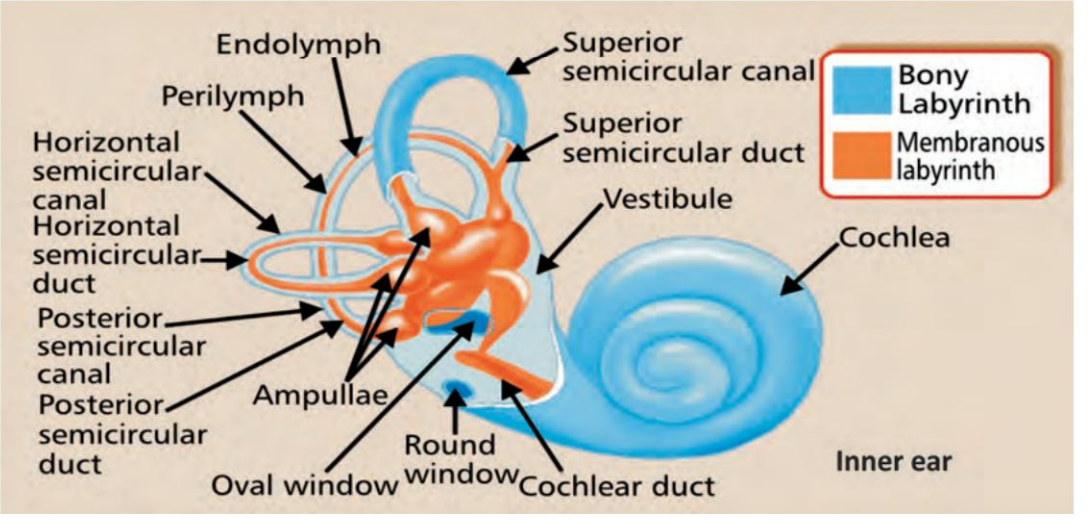
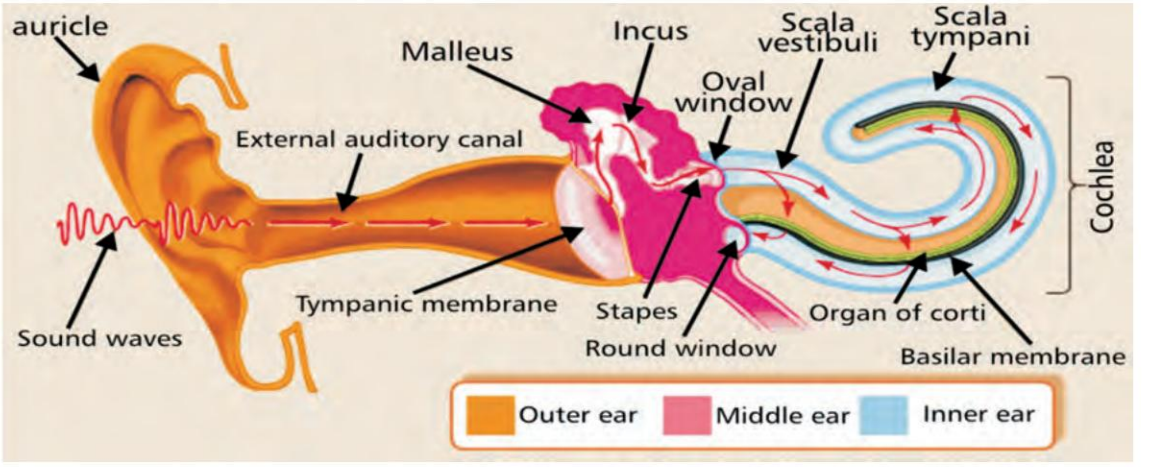


Fig. 11.10



Physiology of hearing

Fig. 11.11

Chapter 12 Endocrine System

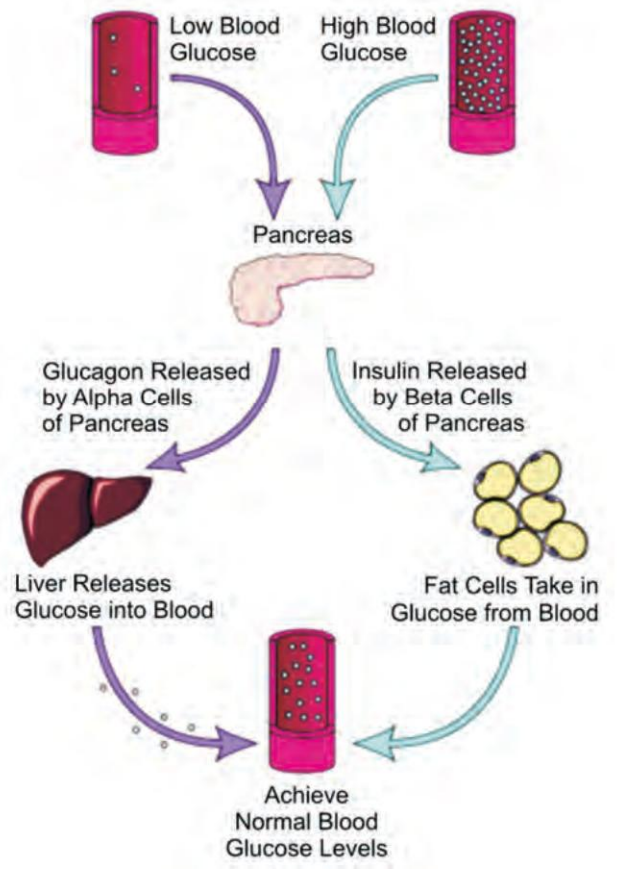
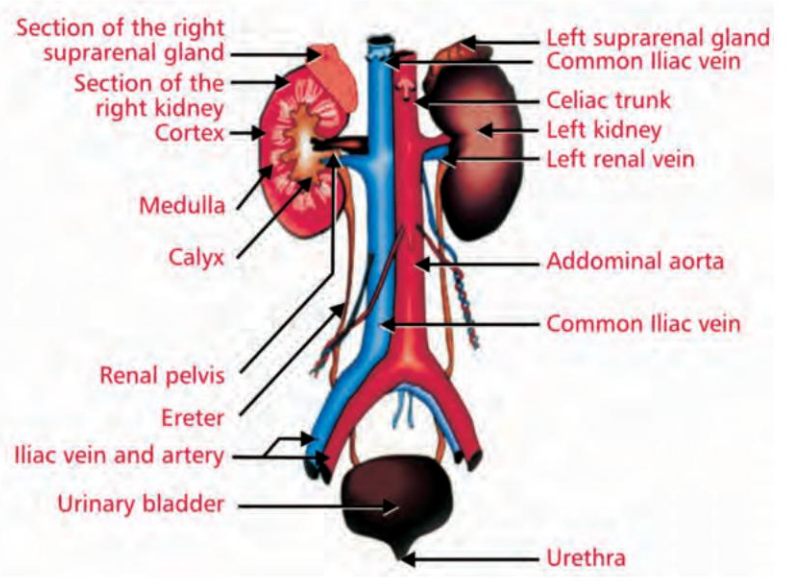


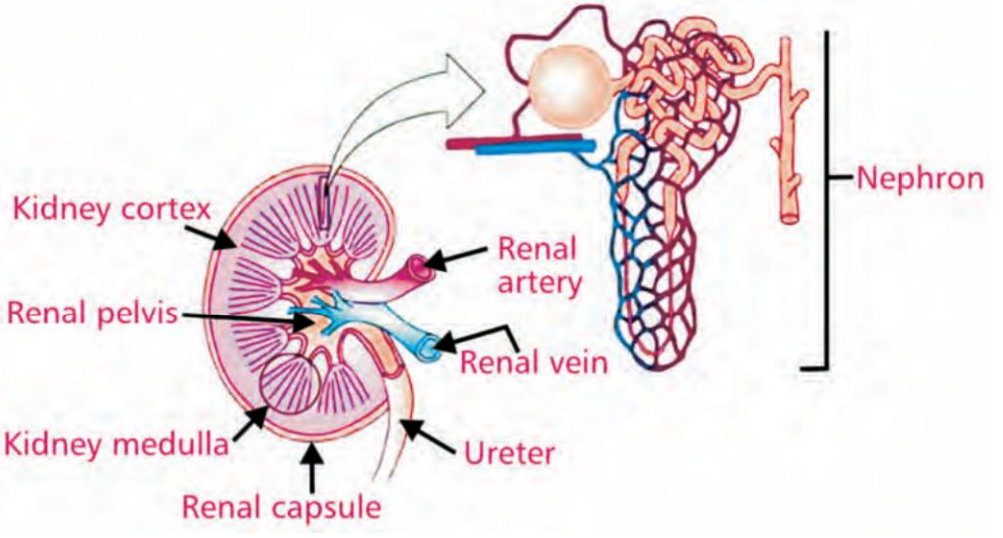
Fig. 12.24

Chapter 13 Excretory System



Urinary system

Fig. 13.1



Structure of kideny

Fig. 13.2

Chapter 15 Blood

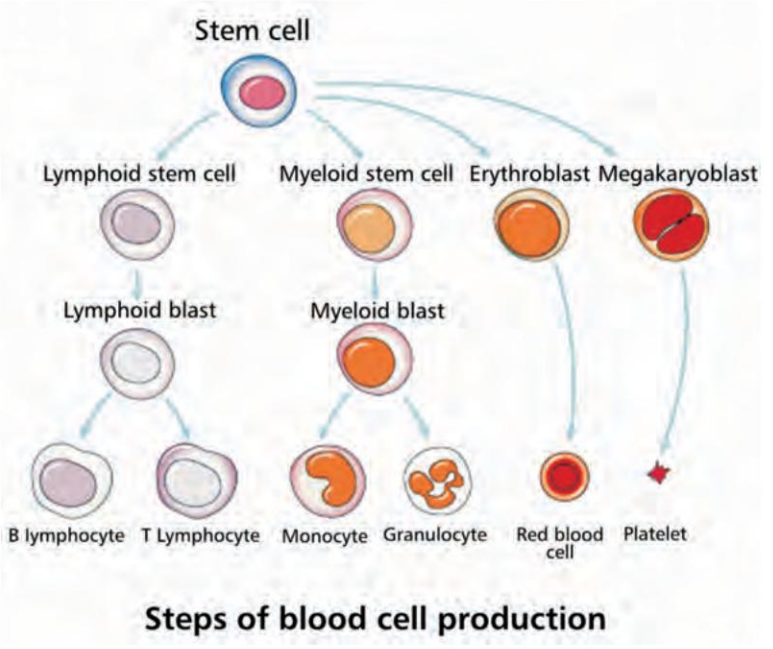
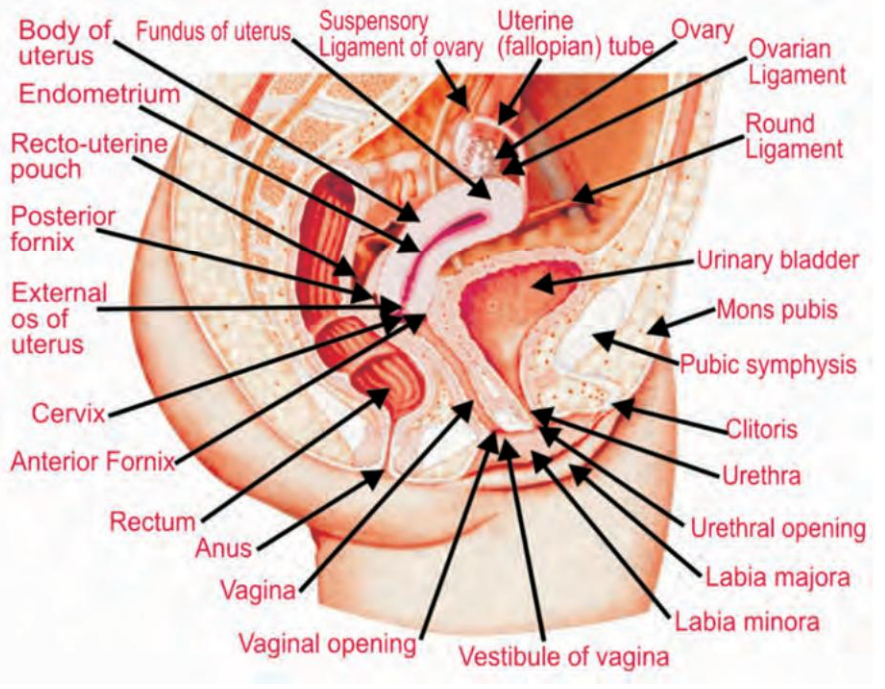


Fig. 15.9

Chapter 16 Reproductive System



Female genital organs (vertical section)

Fig. 16.2

The McGraw·Hill Companies

Chapter

1 Scope of Anatomy and Physiology

- **ANATOMY**
  - Structural organization
    - Organ system
      - Regionally
      - Systemically
      - Scientifically
  - Anatomical terms
    - Directional
    - Regional
    - Body planes
  - Cavities of the body
    - Ventral
      - Thoracic
        - Mediastinal
        - Pleural
      - Abdominopelvic
        - Abdominal
        - Pelvic
    - Dorsal
      - Cranial
      - Spinal
- **PHYSIOLOGY**
  - Homeostasis
    - Maintenance of homeostasis of various variables
    - Role of various systems in maintaining homeostasis
    - Mechanism
      - Negative feedback
      - Positive feedback
  - Acid–base balance
    - Buffer system
    - Respiratory system
    - Role of kidneys
      - Causes of acidosis
      - Causes of alkalosis

Introduction

Medicine has evolved dramatically over the past century. The advent of molecular biology, sophisticated new imaging techniques and advances in information technology have contributed to an explosion of scientific information that has fundamentally changed the way we define, diagnose, treat and prevent disease. This explosion of scientific knowledge is not at all static, as it continues to intensify with time.

The application of the modern scientific methods in the field of medicine has changed the scenario in diagnosing diseases and hence, there is a need to have better treatment. Herein comes the role of a pharmacist in finding newer and better molecules (drug) for treatment.

Pharmacy is a health-care profession that links health sciences with chemical sciences and ensures services related to health care, including clinical services, reviewing medications for safety and efficacy and providing drug information. Pharmacists, therefore, are experts on drug therapy and are the primary health-care professionals who, with the guidance of a medical doctor, also, dispense drugs to a patient. So a pharmacist is a link between a patient and a treating doctor.

Unless he/she is aware about the normal functioning of biological systems in the human body, a pharmacist cannot understand the role of a particular drug molecule to be used for a particular disease, where an organ or a particular system is not functioning properly.

And to do so and to keep pace with ever-advancing medical science, a pharmacist has to have a basic knowledge about the structure (anatomy) and functioning (physiology) of the human body.

1.1 ANATOMY

Anatomy is a branch of biology, which means the study of the structure of a living body. It is subdivided into **macroscopic anatomy** (gross anatomy) and microscopic anatomy. Gross anatomy is the study of anatomical structures that can be seen by unaided vision. **Microscopic anatomy** is the study of minute anatomical structures viewed with microscopes, which includes **histology** (the study of tissues) and **cytology** (the study of cells).Thus, human anatomy, including gross human anatomy and histology, is primarily the scientific study of the morphology of the adult human body.

Superficial anatomy, or **surface anatomy**, is the study of anatomic structures that can be identified on the outside of the body. **Applied anatomy** is a direct application of the facts of human anatomy to the various pathological conditions. **Embryology** is the study of the various stages of intra-uterine development from the fertilized ovum up to the period when it assumes the position of a fully formed fetus.

Generally, students of certain biological sciences, paramedics, physiotherapists, nurses and medical students learn gross anatomy and microscopic anatomy from anatomical models, skeletons, textbooks, diagrams and tutorials. The study of microscopic anatomy (histology) can be aided by examining histological preparations (slides) under a microscope. A medical student, also, learns gross anatomy with practical experience of dissection and inspection of cadavers (dead human bodies).

1.1.1 Structural Organisation

The human body has the most complex structural organization, where the cell is the basic unit for its functioning.

It begins at the chemical level, viz., the **atoms**, which combine with one another to form a **molecule.** Different molecules combine to form organelles, which are the structural and functional components of a cell. The **cells**, as mentioned above, are the smallest, independent units of the human body. They can be seen and studied only by using a microscope, as they are too small to be seen with the naked eye. Clusters of cells become specialized to carry out specialized functions. The cells with similar structure and functions combine to form a **tissue**. Different types of tissues combine to form a structure called an **organ**, the function of which is to carry out a specialized task. Various organs, in conjunction with each other—carrying out a special function, e.g., digestion—is called an **organ system**.

1.1.2 Organ System

Human anatomy can be studied in the following ways:

1. REGIONALLY: Studying Anatomy by Bodily Regions

The human body is divided into several major regions, viz, head, trunk, upper limbs and lower limbs.

The **head** consists of the skull (contains the brain) and face (includes eyes, nose, ears, mouth, forehead, cheeks and chin).

The **neck** supports the head and is attached to the trunk.

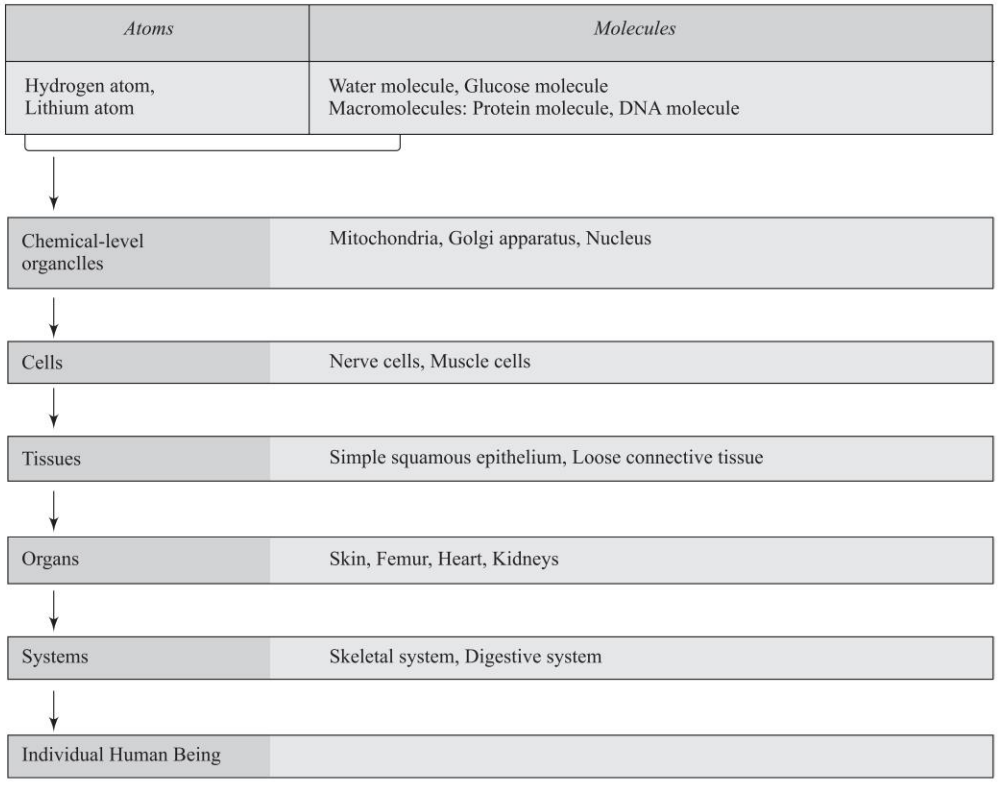
The **trunk** consists of the chest, abdomen and pelvis.

Upper limbs consist of shoulders, armpits, arms, forearms, wrists and hands.

Lower limbs consist of buttocks, thighs, legs, and feet.

The **groin** is the area on the front surface of the body marked by a crease on each side where the trunk joins the legs.

Table 1.1 *Structures of the human body*



2. *SYSTEMICALLY: Studying Anatomy by Specific Systems*

Table 1.2 *Different organ systems and their components and functions*

Organ System	*Components*	*Function*
Integumentary	Skin, Hair, Nails	Protection
Skeletal	Bones	Support/Protection
Nervous	Brain, Spinal cord, Nerves, Sense organs	Receive/Transmit impulses
Muscular	Muscles	Movement
Endocrine	Pituitary, Thyroid, Parathyroid, Pineal, Thymus, Adrenal, Pancreas, Ovary and Testes	Metabolism/Homeostasis
Cardiovascular	Heart, Blood, Blood vessels	Transport
Lymphatic	Lymph vessels and lymph nodes	Transport/Cleanses blood
Respiratory	Nose, Pharynx, Larynx, Trachea, Lungs	Gas exchange
Digestive	Mouth, Esophagus, Stomach, Pancreas, Gall Bladder, Intestines and Colon	Breakdown and absorption of foods
Urinary	Kidneys, Ureters, Bladder, and Urethra	Waste processing and elimination
Reproduction	Gonads	Propagation

3. SCIENTIFICALLY: Studying Anatomy by Specific Sciences

Table 1.3 *Different anatomical sciences*

Osteology	Bony system, skeleton
Syndesmology	Articulation or joints
Myology	Muscles, Fascie
Angiology	Vascular system comprising the heart, blood vessels, lymphatic vessels, lymph glands
Neurology	Nervous system; Organs of sense may be included
Splanchnology	Visceral system, i.e., thoracic viscera and abdomino-pelvic viscera; the heart, a thoracic organ, is best considered with the vascular system. The rest of the viscera may be grouped according to their functions, e.g., respiratory, digestive, urogenital including testes and external genital organs.

1.1.3 Anatomical Terms

For descriptive purposes, the body is supposed to be in the erect posture, with the arms hanging by the sides and the palms of the hands directed forward. This is called the **anatomical position** of the body.

If the body is lying face down, it is in the **prone position**.

If the body is lying face up, it is in the **supine position**.

Anatomical nomenclature, such as regional names and directional terms (planes, sections), enable learners to precisely describe the relationship of one body structure to another.

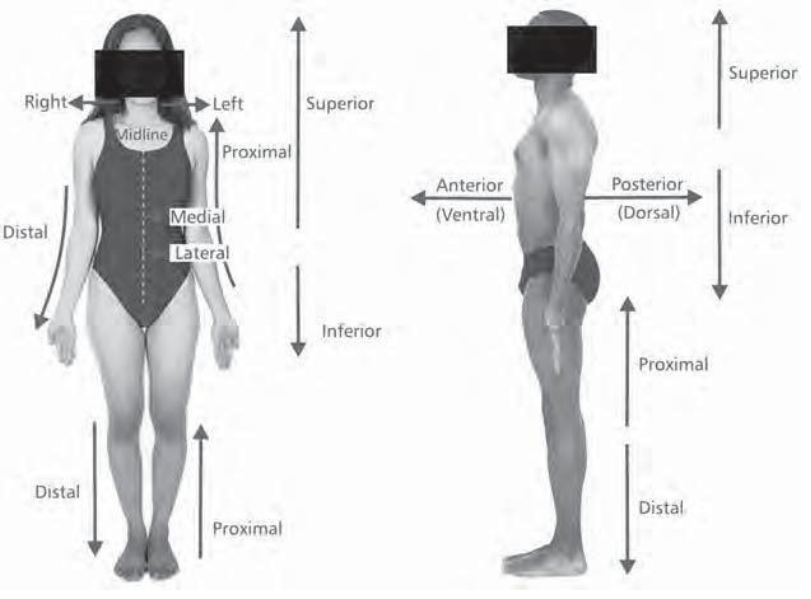


Fig. 1.1 *Directional terms*

1. Directional Terms

Table 1.4 *Directional terms and their explanations*

Term	*The part of the body is being described as*	*Examples*
Anterior or Ventral	Nearer to the front of the body	• The pharynx is anterior to the vertebrae.
	toward the front	• The face is on the ventral surface of the head.
Posterior or Dorsal	After, behind or	• The esophagus is posterior to the trachea.
	toward the back	• The vertebral column is on the dorsal surface.
Superior or Cranial	Above, over, higher, at an upper level	The larynx is superior to the trachea.

(*Contd*)

(*Contd*)

Inferior or Caudal	Below, under, down, at a lower level	The abdomen is inferior to the thorax.
Proximal	Near, closer to the origin (centre), nearer to an organ or limb or part of a body	Elbow is proximal to the wrist.
Distal	Away from, farther from the origin (centre), farther from attached end of a limb or organ or part of the body	The limbs are distal to the trunk.
Medial	Toward the midline, middle, interior to the side	The eyes rotate medially due to action of medial rectus muscle.
Lateral	Toward the side, away from the midline	The lungs lie in the lateral part of the chest.
Ipsilateral	On the same side of the body	Gall bladder and ascending colon are ipsilateral.
Contralateral	On the opposite side of the body	Ascending and descending colons are contralateral.
Intermediate	Between two structures	Transverse colon is intermediate between the ascending and descending colon.
Superficial	Toward or on the surface of the body	Ribs are superficial to the lungs.
Deep	Away from the surface of the body	Ribs are deep to the skin of the chest and back.
Parietal	Associated with the body wall	
Visceral	Associated with organs	
External/Internal	Reserved almost entirely for describing the walls of cavities or of the hollow viscera	

2. *Regional Terms*

Table 1.5 *Regional terms and their explanations*

Cephalic	=	head	Brachial	=	arm	Tarsal	=	ankle
Frontal	=	forehead	Antecubital	=	front elbow	Hallux	=	big toe
Nasal	=	nose	Olecranal	=	back elbow	Occipital	=	back of skull
Orbital	=	eye	Ante brachial	=	forearm	Vertebral	=	spinal
Buccal	=	cheek	Popliteal	=	posterior knee	Scapular	=	shoulder blade
Oral	=	mouth	Sural	=	calf	Dorsum	=	back
Cervical	=	neck	Carpal	=	wrist	Lumbar	=	lower back
Mental	=	chin	Palmar	=	palm	Sacral	=	between hips
Acromial	=	shoulder	Pollex	=	thumb	Perineal	=	between anus and genitalia
Sternal	=	breast bone	Digital	=	fingers/toes	Femoral	=	thigh
Axillary	=	armpit	Pubic	=	genital	Calcaneal	=	heel
Thoracic	=	chest	Patellar	=	anterior knee	Plantar	=	sole
Mammary	=	breast	Crural	=	leg			

3. *Body Planes (See Fig. 1.2)*

A body plane is an imaginary flat surface that is used to define a particular area of anatomy.

(a) Sagittal Plane (vertical or antero-posterior plane) It divides the body into right and left halves. The **mid-sagittal plane** (median plane) passes through the midline and divides the body into equal right and left sides, while the **parasagittal plane** is off to one side and divides the body into unequal right and left regions.

(b) Coronal Plane or Frontal Plane It is the plane which is at right angles to the median plane and divides the front and back halves of the whole body.

(c) Axial Plane or Transverse Plane The transverse planes divide the body into upper (superior) and lower (inferior) regions.

1.1.4 Cavities of the Body

The cavities, or spaces, of the body contain the internal organs, or viscera.

There are two main cavities—the ventral and the dorsal cavities.

1. *Ventral Cavity*

It is the larger cavity and is subdivided into two parts:

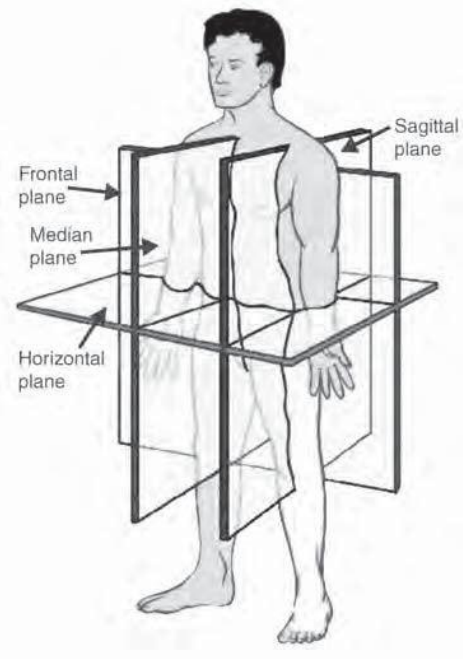


Fig. 1.2 *Body planes*

- Thoracic cavity
- Abdominopelvic cavities

Both are separated by the diaphragm, a dome-shaped respiratory muscle.

(a) Thoracic Cavity The upper ventral, thoracic, or chest cavity is further divided into

- *Mediastinal Cavity* Contains the heart, trachea, large blood vessels and nerves

- *Pleural Cavity* Contains the lungs

The thoracic cavity is bound laterally by the ribs (covered by costal pleura) and the diaphragm caudally (covered by diaphragmatic pleura).

(b) Abdominopelvic Cavities The lower part of the ventral (abdominopelvic) cavity can be further divided into two portions:

- Abdominal portion
- Pelvic portion

Abdominal Portion The abdominal cavity contains the liver, gall bladder, spleen, stomach, pancreas, small intestine, parts of large intestine, the kidneys and adrenal glands.

The abdominal cavity is bound cranially by the diaphragm, laterally by the body wall, and caudally by the pelvic cavity.

There are nine regions (quadrants) of the abdominopelvic cavity:

- The top horizontal, the **subcostal line**, is drawn just inferior to the rib cage.

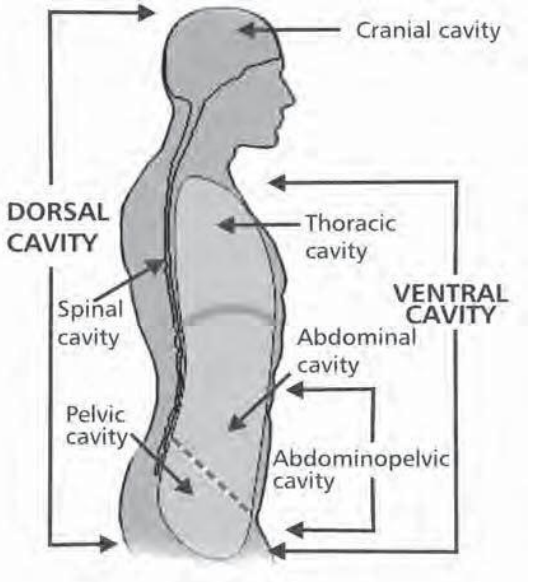


Fig. 1.3 *Body cavities*

- The bottom horizontal, the **transtubercular line**, is drawn just inferior to the tops of the hip bones.
- Two vertical lines, the left and right, **midclavicular lines**, are drawn through the midpoints of the clavicles.

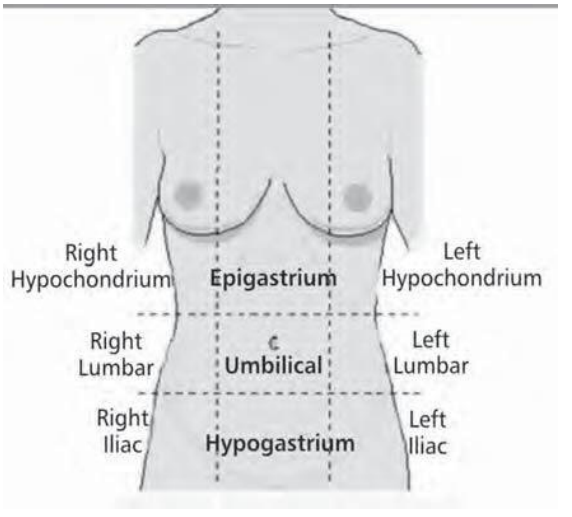


Fig. 1.4 *Abdominal regions*

Thus, the nine quadrants formed are the right and left hypochondria, the right and left lumbar regions, the right and left iliac fosse, epigastrium, umbilical region and hypogastrium.

Pelvic Portion The pelvic cavity contains the sigmoid colon, rectum and most of the urinary bladder and the reproductive organs.

The pelvic cavity is bounded cranially by the abdominal cavity, dorsally by the sacrum, and laterally by the pelvis.

2. *Dorsal Cavity*

The smaller of the two main cavities is called the dorsal cavity. The dorsal cavity, again, can be divided into two portions.

- The upper portion or the cranial cavity houses the brain,
- The lower portion, or vertebral canal, houses the spinal cord.

1.2 PHYSIOLOGY

Physiology is the study of life. It helps us understand how the body parts work together—from the smallest part (cells) all the way to the whole body, for example, the heart, lungs, and muscles must all work together perfectly to allow an athlete to run and jump.

It also helps us understand how our body reacts to different environmental conditions. Whether the weather is very hot or very cold, the body has ways to help the inside of the body stay at just the right temperature.

It helps us understand how living creatures do all the things they do, e.g., eat, sleep, run, jump, even breathe and keep their hearts beating!

The biological basis of the study of physiology refers to the overlap of many functions of the various systems of the human body. It is achieved through communication of different systems with each other, which occurs in a variety of ways, both electrically as well as chemically.

Physiology is the study of these systems' integrated functions and the processes by which they maintain the internal environment.

Traditionally, a student has to view the body as a collection of interacting systems, each with its own combination of functions and purposes. These systems are the nervous system, musculoskeletal system, circulatory system, respiratory system, gastro-intestinal system, urinary system, reproductive system, immune system and endocrine system.

The traditional divisions by system are somewhat arbitrary. Many body parts participate in more than one system. In particular, is the **neuroendocrine system**, where the complex interactions of the neurological and endocrinological systems together regulate physiology. The study of how physiology is altered in disease is **pathophysiology**.

Thus, anatomy and physiology are closely related fields of study: anatomy, the study of form; and physiology, the study of function, are intrinsically tied and are studied in tandem as part of a medical curriculum.

1.2.1 Homeostasis

Cells in the body work best when their surroundings are kept constant. Living cells can function only within a narrow range of variation of the environment factors such as temperature, pH, ion concentrations, and nutrient availability. But one is exposed to ever-changing environmental conditions. Living organisms must survive in an environment where these and other conditions vary from hour to hour, day to day, and season to season. Organisms, therefore, require mechanisms for maintaining internal stability in spite of environmental change.

The ability or tendency of an organism or a cell to maintain internal equilibrium by adjusting its physiological processes is called homeostasis.

In other words, homeostasis means the body's ability to physiologically regulate its inner environment in response to fluctuations in the outside environment and the weather. Literally, it means 'unchanging' but practically it means a dynamic, ever-changing situation, kept within narrow limits. When the balance gets disturbed or lost then the well-being of the individual is threatened.

The processes and activities that help maintain homeostasis are referred to as **homeostatic mechanisms**.

The body has many mechanisms that keep the cell surroundings constant even though the external environment is changing.

Maintenance of Homeostasis

Apart from other systems, the autonomic nervous system and the endocrine system play a major role in maintaining the internal homeostasis. The autonomic nervous system brings about rapid changes and the hormones of the endocrine system bring about slower adjustments.

The following are the examples of how various variables are maintained by various mechanisms of homeostasis.

1. The normal **pH** of extracellular fluid is 7.4. Both decrease in pH, i.e., **acidosis**, or increase in pH, i.e., **alkalosis**, affects the tissues.

   The concentration of ions in relation to one another (e.g., Na^+, K^+, H^+) determine the body's pH, which is closely regulated by the respiratory and urinary systems.

   The kidneys are responsible for regulating blood and water levels, by their function of re-absorption of essential materials and removing wastes from the blood along with water.

   It is the kidneys that remove H^+ ions and other components which help in maintaining salt and ion levels in the blood.

   The most important way that the pH of the blood is kept relatively constant is by the help of buffers dissolved in the blood**.** Other organs also help enhance the homeostatic function of the buffers.

   Acidosis that results from failure of the kidneys to perform this excretory function is known as **metabolic acidosis**.

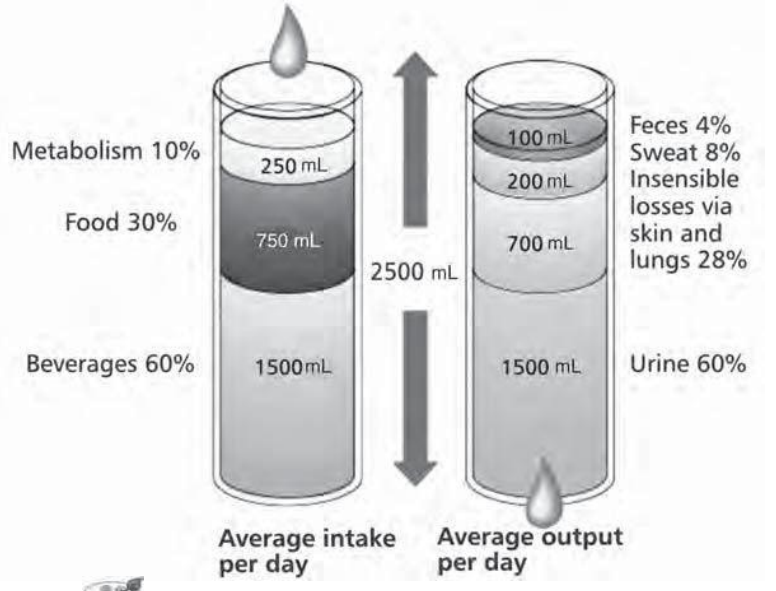


Fig. 1.5 *Fluid homeostasis (Refer colour figure)*

Acidosis that results from failure of the lungs to eliminate CO_2 as fast as it is produced is known as **respiratory acidosis**.

Excretion by the kidneys is a relatively slow process, and may take too long to prevent acute acidosis, e.g., during exercise, there is excessive collection of CO_2, leading to a fall in pH and hence the acidosis. The lungs provide a faster way to help control the pH of the blood. The increase in the rate and depth of breathing in response to exercise helps in removing CO_2 (a component of the principal pH buffer in the blood) and counteract the pH-lowering effects of exercise.

2. Normal **body temperature** is 37°C. Whenever the temperature rises or falls, the metabolic activities of the cells get altered. **Thermoregulation** is an important aspect of human homeostasis.

   Various systems are involved in this, viz., the excretory system, respiratory system, nervous system, skin, digestive system and skeletal system. Heat is mainly produced by the liver and by muscle contractions.
3. **Nutrients** should be supplied adequately, as they supply energy for the various activities of the cells. They are also necessary for the growth of tissues. Nutrients have to be digested, absorbed into the blood and supplied to the cells. Here, the main role is played by the digestive system and the circulatory system.
4. **Oxygen** has to be supplied and **carbon dioxide** and other **metabolic waste products** have to be removed.

   In this, the main role is played by the respiratory system, excretory system, digestive system and skin.
5. When the **osmolality** of body fluids is altered by dehydration or waterlogging, then, the kidneys, skin, digestive system and salivary glands act to maintain water and electrolyte balance.

   Osmoregulation keeps the body's fluids from becoming too dilute or too concentrated. Osmotic pressure is a measure of the tendency of water to move into one solution from another by a process called **osmosis**. The higher the osmotic pressure of a solution, the more water moves into the solution.

   The kidneys are used to remove excess ions from the blood through urine, thus maintaining the osmotic pressure.
6. **Blood-glucose** levels are kept within a narrow range by various homeostatic mechanisms.

   There are two types of antagonistic metabolic hormones affecting blood glucose levels:
   - **Catabolic hormones** (such as glucagon, growth hormone, cortisol and catecholamine) which increase blood glucose
   - One **anabolic hormone** (insulin) which decreases blood glucose
7. One more example of a negative feedback loop is the regulation of **blood pressure**. An increase in blood pressure is detected by receptors in the blood vessels that sense the resistance of blood flow against the vessel walls. The receptors relay a message to the brain, which in turn sends a message to the effectors, the heart and blood vessels. The heart rate decreases and blood vessels increase in diameter, which cause the blood pressure to fall back within the normal range or set point. Conversely, if blood pressure decreases, the receptors

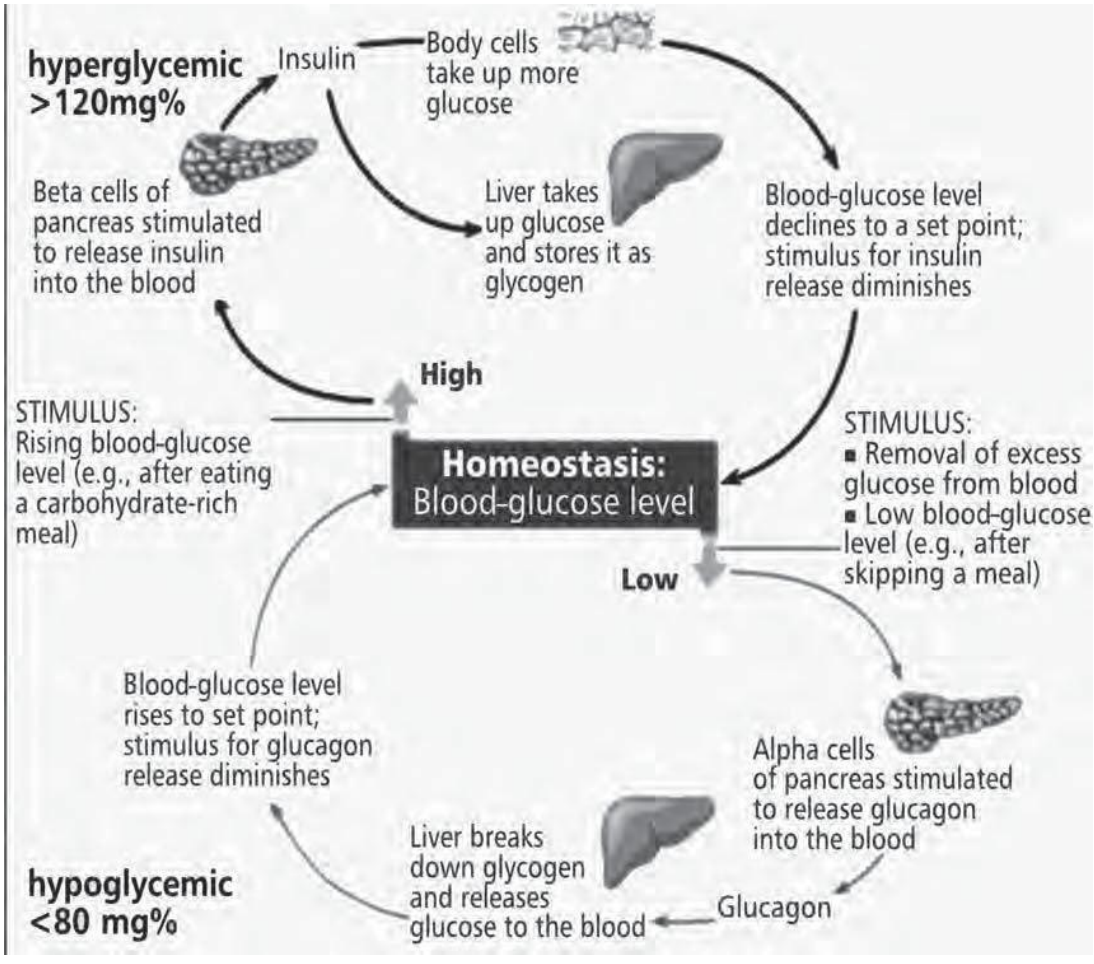


Fig. 1.6 *Homeostasis: Blood-glucose level*

relay a message to the brain, which in turn causes the heart rate to increase, and the blood vessels to decrease in diameter.

Role of Various Systems in the Detection of Changes in the Environment and in Maintaining a Normal Environment

1. **Endocrine glands** play an important role in maintaining homeostasis. Hormones have to act on the body cells appropriately and are essential for the metabolism of nutrients and other substances. Most homeostatic regulation is controlled by the release of hormones into the bloodstream. Hormones alter the metabolism of target organs by increasing or decreasing their activity. These changes in activity are strictly balanced to maintain homeostasis.

   The major causes to which the endocrine glands respond include responses to stress and injury, growth and development, absorption of nutrients, energy metabolism, water and electrolyte balance, reproduction, birth, and lactation.
2. **Blood** forms a major part in the maintenance of internal environment. The red blood cells must be in adequate number with normal shape and size. The composition of plasma should be normal. Blood helps in transporting nutritive substances, oxygen and carbon dioxide and in taking away the metabolic waste products to the necessary organs of excretion.
3. The **central nervous system** also plays a very important role in the human body. The sensory system notices the changes in the body's surroundings and the brain interprets the message and gives the necessary instructions to the motor system to correct the situation accordingly.
4. The **autonomic nervous system** regulates all the vegetative functions of the body, essential for homeostasis.
5. When body temperature falls, **skeletal muscles** are stimulated and lead to shivering and help raise the temperature.

Skeletal muscles also have an important role in the maintenance of normal glucose homeostasis and in regulating whole-body carbohydrate metabolism.

6. **Skin** functions in homeostasis include protection, regulation of body temperature, sensory reception, water balance, synthesis of vitamins and hormones.

Mechanism of Action

All the systems involved in homeostasis operate through two mechanisms which are called feedback mechanisms:

(a) Negative feedback mechanism
(b) Positive feedback mechanism

(a) Negative Feedback Mechanism The usual means of maintaining homeostasis is called a **negative feedback loop**. The body senses an internal change and activates mechanisms that reverse, or negate, that change.

Negative feedback loops require a receptor, a control center, and an effector.

A **receptor** is the structure that monitors internal conditions.

In most homeostatic mechanisms, the **control center** is the brain.

Effectors are muscles, organs, or other structures that receive signals from the brain or control center.

Receptors sense changes in the function and initiate the body's homeostatic response. These receptors are connected to a control center that integrates the information fed to it by the receptors. When the brain receives information about a change or deviation in the body's internal conditions, it sends out signals along nerves. These signals prompt the changes in function that correct the deviation and bring the internal conditions back to the normal range.

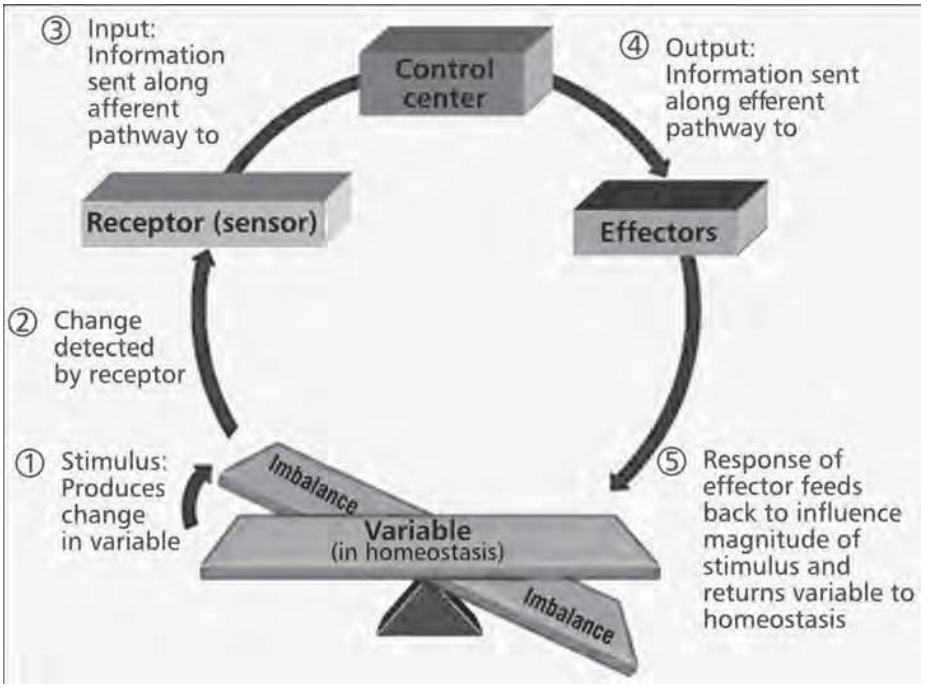


Fig. 1.7 *Mechanism of homeostasis*

(i) This regulatory mechanism will reduce the activity of a particular system whenever its activity increases abnormally, e.g., when thyroxine secretion increases, it inhibits the secretion of Thyroid Stimulating Hormone (TSH) from the pituitary and this, in turn, decreases or stops the secretion of thyroxine from the thyroid gland.

(ii) Another example of negative feedback is body-temperature regulation. If blood temperature rises too high, this is sensed by specialized neurons in the hypothalamus of the brain. They signal other nerve centers, which in turn send signals to the blood vessels of the skin. These blood vessels dilate and more blood flows close to the body surface and excess heat radiates from the body. If this is not enough to cool the body back to its set point, the brain activates sweating. Evaporation of sweat from the skin has a strong cooling effect and the temperature returns to normal.

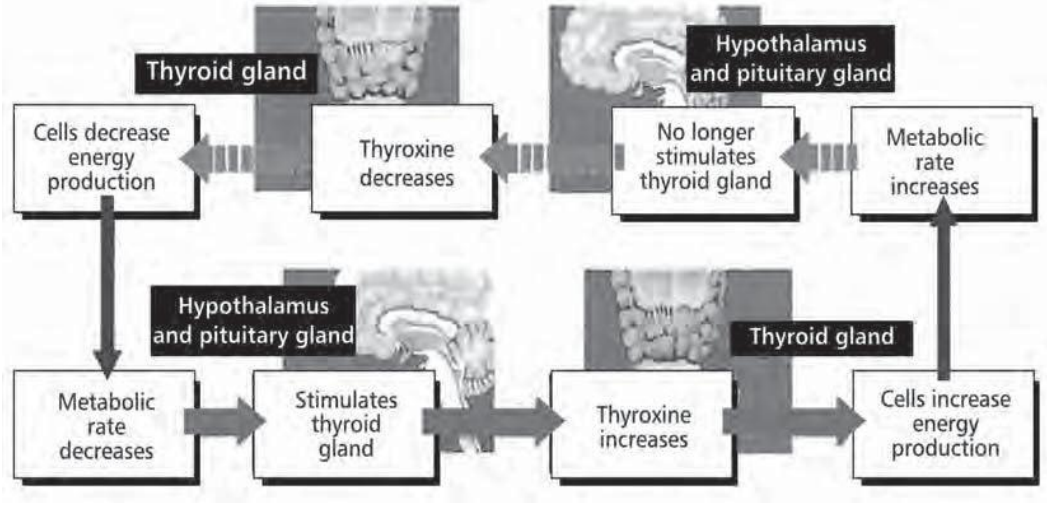


Fig. 1.8 *Regulatory mechanism involving thyroxine secretion*

Fall in temperature is sensed by the hypothalamus in the brain and signals are sent to the cutaneous arteries (message through adrenals) to constrict them. Warm blood is then retained deeper in the body and less heat is lost from the surface. If this is not enough, the brain activates skeletal muscles for shivering and producing heat. This warms the body and the temperature returns to normal.

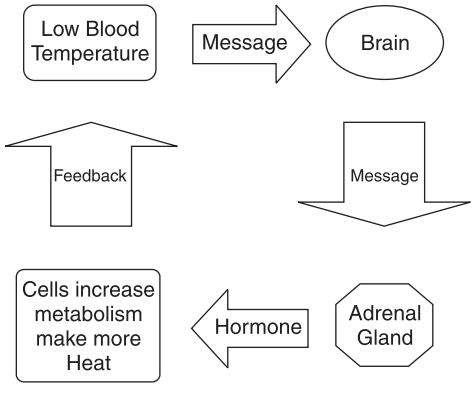


Fig. 1.9 *Homeostasis of temperature*

In both instances, specialized neurons sense the abnormal body temperature and activate corrective negative feedback loops that return the temperature to normal. Thus, the body temperature seldom fluctuates more than 0.5 degrees Celsius above or below its set point.

(iii) Other negative feedback loops regulate blood-sugar concentration, water balance, pH, and countless other variables. These loops are regulated either by the nervous system or by the hormones of the endocrine system. The endocrine system uses cycles and negative feedback to regulate physiological functions. Negative feedback regulates the secretion of almost every hormone:

(b) Positive Feedback Mechanism The counterpart to negative feedback is the positive feedback loop, a process in which the body senses a change and activates mechanisms that accelerate or increase that change.

Only a few systems are involved in positive feedback mechanism as compared to the negative feedback mechanism.

Positive feedback mechanism occurs during secretion of oxytocin, process of blood coagulation, milk-ejection reflex and in labor.

An enzyme is produced that not only forms the matrix of the blood clot, but also accelerates the production of more thrombin. It has a self-accelerating effect, so that once the clotting process begins, it runs faster and faster, until bleeding stops. Thus, this positive feedback loop is part of a larger negative feedback loop. It is activated by bleeding and ultimately works to stop the bleeding.

Another example of beneficial positive feedback is seen in childbirth. When the uterine contractions start, stretching of the uterus leads to the secretion of a hormone, oxytocin, which stimulates uterine contractions and leads to more and stronger contractions that speed up labor. This positive feedback mechanism plays an important role in producing an increased number of uterine contractions during labor. Once labor is over, oxytocin is no longer released and contractions stop.

Yet another function is seen in protein digestion, where the presence of partially digested protein in the stomach triggers the secretion of hydrochloric acid and pepsin, the enzyme that digests protein. Once digestion begins, it becomes a self-accelerating process.

Thus, homeostasis has become one of the most important concepts of physiology, physiological ecology, and medicine. Most bodily functions are aimed at maintaining homeostasis, and an inability to maintain it leads to disease and often death.

1.2.2 Acid–Base Balance

Maintenance of acid–base balance is essential for normal functioning of the cells.

Normal pH of arterial blood is 7.4 and normal pH of venous blood is 7.35.Venous blood is more acidic because of greater proportion of CO_2 and increase in H-ion concentration. Homeostasis of H-ion concentration within a narrow range is necessary for survival.

If the pH falls below 7.4, it is called **acidosis**, which could be due to gain of acid and/or loss of alkali.

Increase in pH of more than 7.4 is called **alkalosis**. It is due to loss of acid and/or addition of base.

Intracellular pH for various cells ranges between 6 and 7.4.

In severe acidosis, blood pH falls below 7.0; and in severe alkalosis, it may rise above 7.5.

Maintenance of acid–base balance is important for homeostasis. Metabolic processes of the body form mostly acidic substances:

1. Oxidation of carbon of food produces CO_2.
2. Oxidation of sulphur containing amino acids results in formation of sulphuric acid.
3. Incomplete oxidation of carbohydrate and fat give rise to ketone bodies.
4. Catabolism of phospho-lipids and phospho-amino acids forms phosphoric acid.
5. In hypo-volemic shock and other forms of circulatory shock, there is anaerobic glycolysis leading to lactic-acid accumulation.
6. Severe exercise leads to lactic-acid accumulation and may cause lactic acidosis due to anaerobic metabolism.
7. In diarrhea, a large amount of bicarbonates with fluid is lost, which is the most frequent cause of metabolic acidosis.
8. In diabetes, as glucose is not utilized, lipids are used for liberation of energy, leading to accumulation of aceto-acetic acid and beta hydroxyl butyric acid. This is called **keto-acidosis**.
9. In renal disease, there is acidosis due to failure to excrete metabolic acids, especially uric acid.

Regulation of normal pH depends on three major mechanisms:

1. Buffer system
2. Respiratory system
3. Kidneys

1. Buffer System

All the body fluids have buffer agents that combine with an acid or base and prevent change in the pH. Thus, optimal pH is maintained by the balance between acids and bases produced by the cells.

Buffer systems are the first line of defense, which act within seconds. They are proteins, phosphates and bicarbonates. They maintain the H-ion concentration within normal limits. Some buffers bind the H ions and thus remove them from circulation. These substances are called the **alkali reserves** of the blood.

Proteins are the major factors among the buffers in the body because of their high concentration in the cells. They are composed of amino acids, which contain the carboxyl group (COOH) and at least one amino group (NH_2).

The carboxyl group acts like an acid and reacts with excess hydroxide to form water.

When pH falls, the amino group reacts with a base.

Thus, proteins can buffer both acids and bases.

The protein **hemoglobin** is an effective method for buffering carbonic acid in the blood. When blood passes through the tissues, carbon dioxide comes out of the cells and enters the blood. In the red blood cells it combines with water to form carbonic acid. Carbonic acid (H_2CO_3) ultimately dissociates into H+ and HCO_3.

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

Oxygen from the blood enters the cells simultaneously and oxyhemoglobin gets reduced to deoxyhemoglobin which picks up most of the H^+.

The **phosphate buffer system** operates in the internal fluid of all cells. This buffer system consists of dihydrogen phosphate ions ($H_2PO_4^-$) as **hydrogen-ion donors (acid)** and hydrogen phosphate ions (HPO_4^{2-}) as **hydrogen-ion acceptors (base)**. These two ions are in equilibrium with each other as indicated by the chemical equation below.

$$H_2PO_4^-(aq) \rightleftarrows H^+(aq) + HPO_4^{2-}(aq)$$

If additional hydrogen ions enter the cellular fluid, they are consumed in the reaction with HPO_4^{2-}, and the equilibrium shifts to the left.

$$H^+ + HPO_4^{2-} \rightarrow H_2PO_4^-$$

If additional hydroxide ions enter the cellular fluid, they react with $H_2PO_4^-$, producing HPO_4^{2-}, and shifting the equilibrium to the right.

Thus, dihydrogen phosphate acts as a weak acid and can buffer strong bases. Monohydrogen phosphate acts as a weak base and can buffer H^+ which is released by a strong acid.

The phosphate buffer system is an important mechanism in the kidneys (discussed later).

The **bicarbonate buffer system** is an important system of our body required to maintain acid–base homeostasis.

(Note that H_2CO_3 is carbonic acid and HCO_3 is bicarbonate.)

In this system, carbon dioxide (CO_2) combines with water to form carbonic acid (H_2CO_3), which in turn rapidly dissociates

to form hydrogen ion and bicarbonate (HCO_3–) according to the reaction shown below. The reverse (leftward) reaction is catalyzed by the enzyme **carbonic anhydrase**.

$$CO_2 + H_2O \rightleftarrows H_2CO_3 \rightleftarrows (H+) + HCO_3$$

- If the pH is too high, carbonic acid will donate hydrogen ions (H^+) and the pH will drop.
- If the pH is too low, bicarbonate will bond with hydrogen ions (H^+) and the pH will rise.

Too much CO_2 or too little HCO_3 in the blood will cause acidosis.

The CO_2 level is increased when **hypoventilation**, or slow breathing, occurs, such as in emphysema or pneumonia. Bicarbonate will be lowered by keto-acidosis, a condition caused by excess fat metabolism (diabetes mellitus).

Too much HCO_3 or too little CO_2 in the blood will cause alkalosis.

This condition is less common than acidosis. CO_2 can be lowered by **hyperventilation**, or fast breathing.

So, in summary, if one has respiratory acidosis, the above equation will move to the right. The body's H^+ and CO_2 levels will rise and the pH will drop. To counteract this, the person will breathe more and release H^+. In contrast, if one is going into respiratory alkalosis, the equation will move to the left. The body's H^+ and CO_2 levels will fall and the pH will rise. So the body will try to breathe less to release HCO_3.

Any disturbance of the system will be compensated by a shift in the chemical equilibrium.

Constantly produced CO_2, as a waste product of cellular respiration when cells make energy, is also eliminated by this system. Thus, the buffer system maintains homeostasis by preventing major changes in the pH. This process is extremely important in human physiology. It manages the many acid and base imbalances that can be produced by both normal and abnormal physiology.

But it can act only when acid or alkali can be eliminated from the body with the help of lungs and kidneys.

Lungs excrete CO_2 causing a fall in H-ion concentration and thereby acidosis is corrected. In alkalosis, the respiration rate is reduced leading to rise in CO_2 levels, and thus pH is normalized.

Kidneys form ammonia which combine with acid products of protein metabolism and get excreted.

2. Respiratory System

Homeostasis is maintained by the respiratory system in two ways: gas exchange and regulation of blood pH.

Gas exchange is performed by the lungs by eliminating carbon dioxide, a waste product given off by cellular respiration. As carbon dioxide exits the body, oxygen (needed for cellular respiration) enters the body through the lungs.

$$CO_2 + H_2O– \leftrightarrow H_2CO_3 \leftrightarrow HCO_3 + H^+$$

When there is increase in carbon-dioxide concentration, it will lower the pH. Conversely, decrease in CO_2 concentration in the body fluids will raise the pH.

Change in the H-ion concentration stimulates the respiratory centre in the medulla oblongata, which alters the rate of breathing. Rate of CO_2 removal changes the pH to normal. It is the second line of defense.

Increase in H-ion concentration will increase the rate and depth of respiration. Alveolar respiration will be increased, more CO_2 is exhaled and pH returns to normal.

Thus, the respiratory center acts as a negative feedback controller of H-ion. It also acts vice versa when there is decrease in H-ion concentration.

3. Role of Kidneys

Kidneys control H-ion concentration in the ExtraCellular Fluid (ECF) by excreting either acidic or alkaline urine. It is the third line defense system. Kidneys regulate the extracellular fluid H-ion concentration by secretion of H-ions into the tubules, reabsorbing HCO_3 and producing of new bicarbonate ions.

$$H^+ + HCO_3^- \rightarrow H_2CO_3$$

Formation of ammonia is another important mechanism for acid–base balance.

In **acidosis**, the H-ion concentration in ECF increases ammonia secretion increases in the epithelial cells of all the tubules, which reacts with H ions, to form ammonium ion, which, with chloride ion, is excreted into the urine as NH_4Cl. HCO_3 is reabsorbed and sodium-bicarbonate concentration is increased in the extracellular fluid. So pH shifts to the alkaline side and acidosis is corrected.

In **alkalosis**, there is increased filtration of HCO_3 at the glomerular level. There is increased secretion of H ions and as HCO_3 cannot be reabsorbed without reaction with H ions, more HCO_3 is excreted. The pH shifts to acidic side and alkalosis is corrected.

Excretion by the kidneys is a relatively slow process, and may take too long to prevent acute acidosis resulting from a sudden decrease in pH. For example, during exercise, the lungs provide a faster way to help control the pH of the blood. The increased-breathing response to exercise helps counteract the pH-lowering effects of exercise by removing CO_2, a component of the principal pH buffer in the blood.

Normally, the kidneys remove up to 500 m.moles of acid or base each day. If it is in greater quantity then this enters the body fluid, and severe acidosis or alkalosis results. (See Fig. 1.10)

(a) Causes of Acidosis

- Diseases such as **emphysema** or **kidney failure** reduce the efficiency of the lungs or kidneys, and thus interfere with their ability to regulate acid–alkali balance.

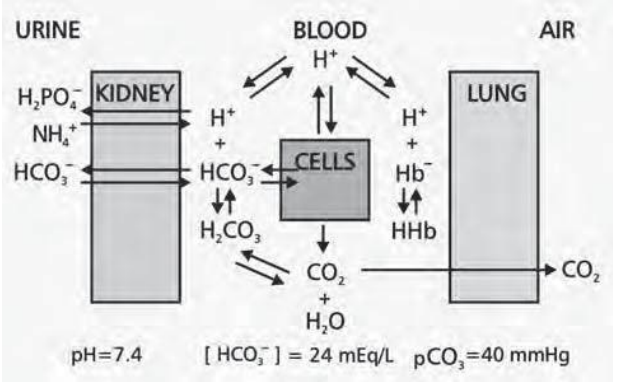


Fig. 1.10 *Acid–base balance*

- **Starvation** and **uncontrolled diabetes** may cause acidosis because of excessive acid produced by metabolism of large amounts of body fat.
- Acidosis is often linked with **increased protein** (meat products) intake.
- Acidosis can also be cause by **ingestion of large amounts of acidic substances.**
- Acidosis can occur as a result of **high fat diet**, which leads to the production of ketones (binds and remove bicarbonate) in the blood.

Metabolic acidosis is due to increased production of H^+ by the body or the inability of the body to form bicarbonate (HCO_3^-) in the kidney or loss of bicarbonate ions from the body, which leads to abnormal increase of acidic metabolic products (other than CO_2).

Diabetic acidosis (diabetic ketoacidosis) develops when substances known as ketone bodies, which are acidic, build up during uncontrolled diabetes

Hyperchloremic acidosis results from excessive loss of sodium bicarbonate from the body, as can happen with severe diarrhea.

Lactic acidosis is a build-up of lactic acid due to alcohol, exercising for a very long time liver failure and medications in excess such as salicylates or aspirin.

Other causes of metabolic acidosis include kidney disease (distal tubular acidosis and proximal renal tubular acidosis), severe dehydration, etc.

Respiratory acidosis results from failure of the lungs to eliminate CO_2, as fast as it is produced.

Reduced CO_2 elimination occurs in decreased respiratory drive (due to drugs or due to central nervous system disorders), e.g., hypoventilation, lung disease and respiratory muscle/nerve disease (myasthenia gravis, botulism, amyotrophic lateral sclerosis, Guillain–Barre syndrome in uncompensated respiratory conditions). The bicarbonate–carbonic acid ratio changes from 20 : 1 to 10 : 1. There is increase in pCO_2 in the blood and carbonic acid.

(b) Causes of Alkalosis

- **Severe diarrhea** may cause alkalosis because of excessive loss of basic fluids.
- Alkalosis may be caused by **loss of carbonic acid** because of rapid breathing.
- Alkalosis can be caused by **excessive vomiting**, resulting in a loss of hydrochloric acid with the stomach content.
- Temporary metabolic alkalosis occurs when there is an **excessive intake of sodium bicarbonate** to relieve acid in the stomach.

Metabolic alkalosis is caused by too much bicarbonate in the blood. It is due to loss of acids from the body or excessive accumulation of alkalis in the blood. Hypochloremic alkalosis is caused by an extreme lack or loss of chloride, which can occur with prolonged vomiting. Hypokalemic alkalosis is caused by the kidneys' response to an extreme lack or loss of potassium, which can occur when people take certain diuretic medications. It is also seen in hyperaldosteronism and Cushing's syndrome.

Respiratory alkalosis is caused by low carbon-dioxide levels in the blood. This can be due to hyperventilation. There is shift of the bicarbonate–carbonic acid ratio to 20:05. This can occur in fever, being at high altitudes, lack of oxygen, anxiety, and aspirin overdose, salicylate poisoning and liver diseases, which makes a person breathe faster.

REVIEW QUESTIONS

1. Discuss the various terms describing the position of the body.
2. Write a note on the anatomical planes.
3. Describe the various cavities of the body.
4. Define homeostasis. How is it maintained?
5. Discuss the role of various systems in the detection of changes in the environment and in maintaining a normal bodily environment.
6. Discuss acid–base balance.
7. Discuss buffer system.
8. Write short notes on:
   (a) Coronal plane
   (b) Organ
   (c) Blood–glucose homeostasis
   (d) Fluid homeostasis
   (e) Acidosis
   (f) Alkalosis
   (g) Positive feedback mechanism
   (h) Negative feedback mechanism
   (i) Structural organization of the human body

Chapter

2 Cell

- **CELL MEMBRANE**
  - Structure
    - Lipid layer
    - Protein layer
    - Carbohydrate layer
  - Functions
  - Transport across the cell membrane
    - Passive transport
      - Diffusion
      - Facilitated diffusion
    - Primary active transport
    - Secondary active transport
    - Vesicle mediated transport
      - Endocytosis
        - Pinocytosis
        - Phagocytosis
        - Receptor mediated endocytosis
      - Exocytosis
  - Ion channels
    - Sodium-channel blocker
    - Potassium-channel blocker
    - Calcium-channel blocker
- **NUCLEUS AND GENETIC MATERIAL**
  - Structure
    - Nuclear membrane
    - Nucleoplasm
    - Nucleoli
    - Genetic material
  - Functions
- **CYTOPLASM**
  - Cell organelles
    - Endoplasmic reticulum
      - Rough and smooth
    - Golgi apparatus

- Lysosomes
- Peroxisomes
- Secretory vesicles
- Mitochondria
- Microsomes
- Centrosomes and centrioles
- Ribosomes
- Cytoskeleton
  - Microtubules
  - Microfilaments
  - Microtrabeculae

• CELL CYCLE

- ○ Interphase
  - Gap 1 or G1 Phase
  - S Phase
  - G2 Phase
- ○ Cell division
  - Mitosis
    - Prophase
    - Metaphase
    - Anaphase
    - Telophase
    - Cytokinesis
  - Meiosis
- ○ Clinical significance

Introduction

The human body is made up of different systems. These systems are made up of tissues. The functioning of these tissues is essential so that the human body remains in the normal state and can carry out its daily activities. These tissues are formed by cells. So the ultimate unit of each system is the cell. If cells die, the tissue dies and the system fails to function. All living matter is made up of cells and the production of new cells goes on from one generation to the other generation.

The biochemical reaction of an organism, that is, its metabolism, takes place in the cells.

A cell is, thus, the structural and functional unit of the living body. Each cell is formed by a cell body, which has two parts—the nucleus and the cytoplasm—and this cell body is covered by a membrane.

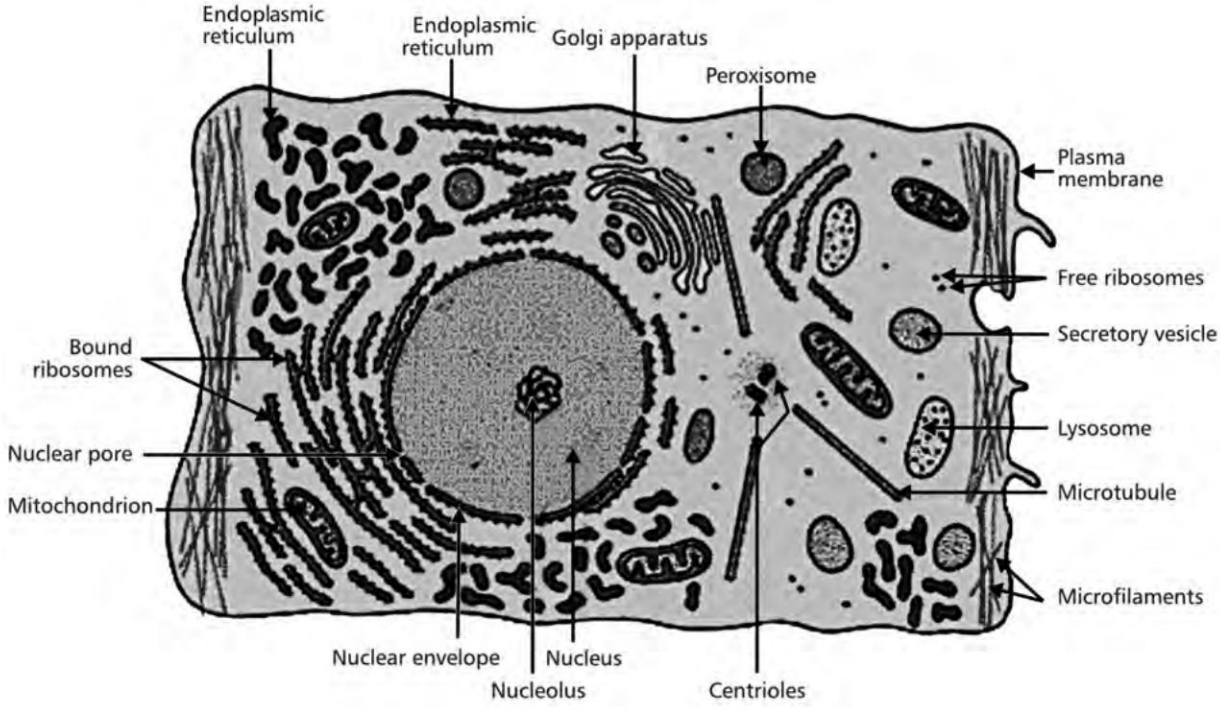


Fig. 2.1 *Structure of the cell*

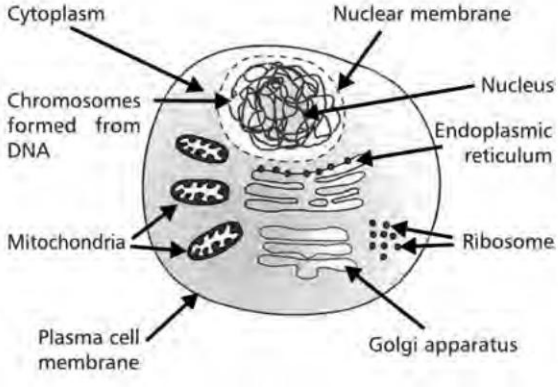


Fig. 2.2 *Structure of the cell (schematic)*

2.1 CELL MEMBRANE

The **cell membrane** (also called the **plasma membrane** or **plasmalemma**) is a biological membrane separating the interior of a cell from the outside environment, i.e., the fluid surrounding the cell, which is the extracellular fluid.

The cell membrane is a fluid mosaic of lipids, proteins, and carbohydrates**.**

According to the fluid mosaic model, the biological membrane can be considered a two-dimensional liquid, where all lipid and protein molecules diffuse more or less freely.

The apical membrane of a polarized cell is the surface of the plasma membrane that faces the lumen. This is particularly evident in epithelial and endothelial cells.

2.1.1 Structure of the Cell Membrane

The cell membrane is a three-layered membrane.

These three layers are

- Central electrolucent layer, called the **lipid layer**, formed by lipid substances.
- Two electron-dense layers, one on either side of the central layer, formed by proteins and some carbohydrate molecules.

1. Lipid Layer

There are two layers of lipid molecules, which cover the entire body of the cell.

Both membranes are flat sheets that form a continuous barrier around the cells. Lipid bilayers are quite fragile and are so thin that they are invisible in a traditional microscope—to be seen, they often require advanced techniques like electron microscopy and atomic force microscopy.

They are usually made, mostly, of phospholipids, which have an electrically charged **hydrophilic** (water-loving) head and two **hydrophobic** (water-hating), tails. When phospholipids are exposed to water, they arrange themselves into a two-layered sheet with all of their tails pointing toward the center of the sheet. The center of this bilayer contains almost no water and also excludes molecules like sugars or salts that dissolve in water but not in oil. Thus, heads project towards the interior and exterior of the membrane, and tails project towards each other and the center of the membrane.

Phospholipids serve a major function in the cells of all organisms. The cholesterol part forms only 25% of the lipid layer. If the cholesterol level increases then the permeability of the cell membrane decreases.

2. Protein Layer

Protein layers are electron dense layers, which cover the two surfaces of the central layer. They are coiled polypeptides and have charged hydrophilic or uncharged hydrophobic groups.

Two types of protein molecules are present.

1. Integral proteins
2. Peripheral proteins

Integral proteins can pass through the cell membrane. The pores get entirely lined by integral protein molecules because the protein molecules invaginate into the pores of the lipid layer from either side. These pores form channels, for diffusion of water, electrolytes and those substances which cannot pass through the lipid layer. The pores are called **hypothetical pores**, and the channels are called **protein channels**.

Integral membrane proteins are permanently attached to the membrane. They can be classified according to their relationship with the bilayer:

- **Transmembrane proteins** spread through the entire length of the membrane
- **Integral monotopic proteins** permanently attached to the membrane from only one side

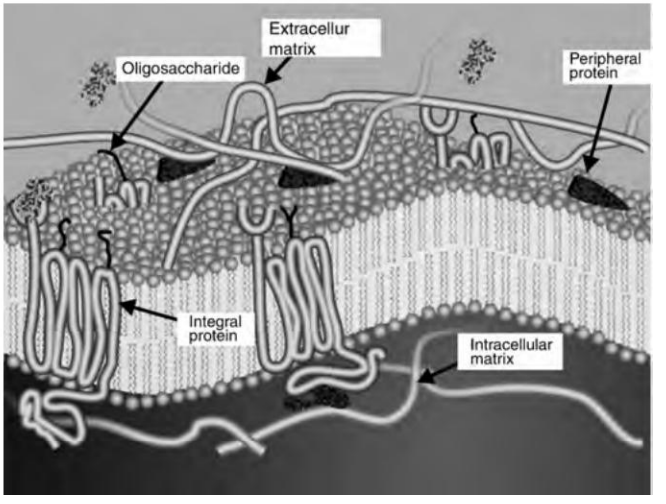


Fig. 2.3 *Cell membrane*

Peripheral proteins are only bound to the surface and neither penetrate the cell membrane nor are they tightly associated with the cell membrane. They are temporarily attached either to the lipid bilayer or to integral proteins.

3. Carbohydrate Layer

Some carbohydrates are attached to proteins or lipids throughout the surface of the cell membrane. With proteins, they form glycoprotein and with lipids, they form glycolipids. A thin covering of carbohydrate molecules, called **glycocalyx**, is formed on the surface of cell membranes.

2.1.2 Functions of the Cell Membrane

1. The function of the cell membrane is to protect the cell by enveloping the cell body. It is a semipermeable membrane, and so free exchange of certain substances takes place between the extracellular and the intracellular fluids. The movement of substances across the membrane can be **passive**, occurring without the use of cellular energy; or **active**, requiring the cell to expend energy in moving substances in/out.
2. The cell membrane supports the cytoskeleton in providing a shape and size to the cell. By virtue of attaching to the extracellular matrix and other cells, they form a group of cells, together to form tissues.
3. The lipid layer allows only fat-soluble substances to pass through it, for example, oxygen, carbon dioxide and alcohol.

   Water-soluble substances like glucose, urea and electrolytes are prevented from going through it.

   This capacity of controlling the passage of substances across it is called **selective permeability**.
4. Bilayers are particularly impermeable to ions, which allow cells to regulate salt concentrations and pH by pumping ions across their membranes, using proteins called **ion pumps**. It keeps ions, proteins and other molecules where they are needed and prevents them from diffusing into areas where they should not go.

   This semipermeable nature of the membrane allows the cell to maintain the composition of the cytosol independent of the external environment.
5. A membrane protein is a protein molecule that is attached to, or associated with, the membrane of a cell or an organelle. Integral proteins provide the structural integrity of the cell membrane. Specific proteins embedded in the cell membrane can act as molecular signals that allow cells to communicate with each other.
6. Transport proteins play an important role in the maintenance of concentrations of ions. These transport proteins come in two forms:
   - Carrier proteins
   - Channel proteins.

   Carrier proteins are involved in using the energy released from ATP while it is being broken down to facilitate active transport and ion exchange.

   These processes ensure that useful substances (oxygen and nutrients) are able to enter the cell and toxic substances (carbon dioxide, metabolites and waste products) are pumped out of the cell. **Channel proteins** form channels for water-soluble substances.
7. Membrane enzymes produce a variety of substances essential for cell function.
8. Protein receptors function to receive signals from both the environment and other cells. These signals are transduded and passed, in a different form, into the cell. For example, a hormone binding to a receptor could open an ion channel in the receptor and allow calcium ions to flow into the cell. Neurotransmitters act after binding to the receptors.
9. Other proteins on the surface of the cell membrane serve as **markers** that identify a cell to other cells. The interaction of these markers with their respective receptors forms the basis of cell–cell interaction in the immune system.
10. Some proteins act as antigens and induce antibody formation.
11. Carbohydrate molecules get bound to proteins on the outside of the membrane and form glycoproteins. These glycoproteins serve as specific receptors for other molecules.

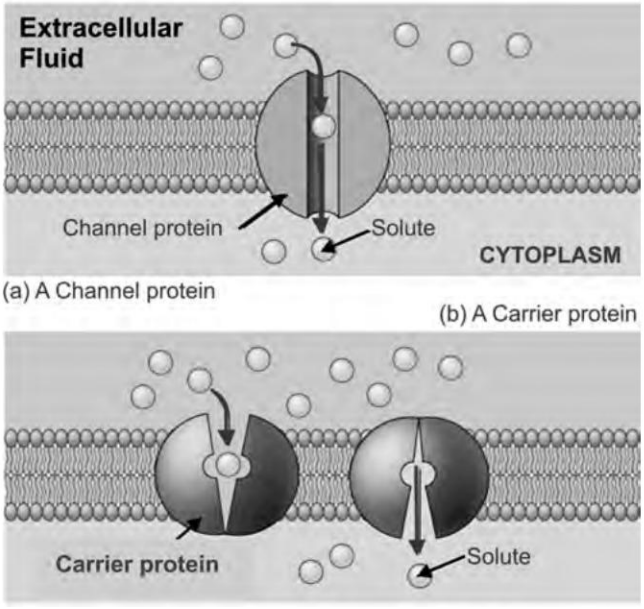


Fig. 2.4 *Carrier proteins and channel proteins*

2.1.3 Transport Across the Cell Membrane

Transport across the plasma membrane is essential to the life of a cell.

- Certain substances must move into the cell to support metabolic reactions.
- Certain substances, produced by the cell for export and the cellular waste materials which accumulate at the end of metabolism must move out.

There are four primary means by which water and other small molecules cross into or out of cells.

1. Passive transport—diffusion and facilitated diffusion
2. Primary active transport
3. Secondary active transport
4. Vesicle mediated transport

Transport across the membrane can take place either with the help of membrane components or without the help of membrane components (e.g., diffusion).

1. Passive Transport

(a) Diffusion Diffusion is a process whereby substances move from an area of higher concentration to an area of lower concentration. It takes place without the help of membrane components.

Diffusion takes place across a semipermeable membrane. The plasma membrane functions as a selectively permeable membrane with specific selectivity regarding which molecules cross and in which direction they are allowed to do so.

The best example is the inability of large protein molecules and red blood cells to cross the capillary walls while water can move in either direction.

Passive transport is helped by the kinetic energy of the molecules itself. There is no expenditure of metabolic energy or no input of energy from the cell.

Water, carbon dioxide, and oxygen are among the few simple molecules that can cross the cell membrane by diffusion.

There are many factors on which diffusion depends:

- Diffusion can be accelerated if concentration of the substance is more.
- The process of diffusion is faster if the temperature rises.
- The thickness of the membrane also affects the process—more the thickness, slower the diffusion.
- If the size of the pore is more, diffusion is faster and the pore size is affected by calcium—increase in calcium level decreases pore size and affects the diffusion of positively charged ions.

Osmosis is the diffusion of water across a semipermeable membrane. This process takes place when diffusion of solutes cannot take place. These membranes are impermeable to organic solutes with large molecules (such as polysaccharides) while being permeable to water and small uncharged solutes. The water molecules pass through the cell membrane from an area of low solute concentration (outside the cell) to one of high solute concentration (inside the cell). This goes on till equilibrium is reached.

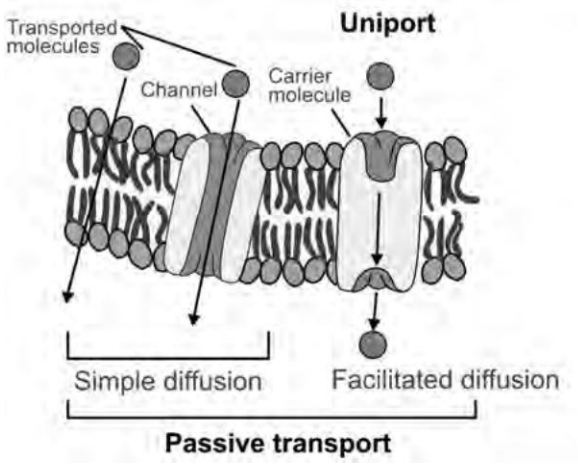


Fig. 2.5 *Passive transport*

For example, this process is necessary for the maintenance of the structure of red blood cells. If plasma becomes more dilute than the fluid in the RBC then the cells will swell up due to movement of fluid into the cell and vice versa leading the red blood cells to shrink.

(b) Facilitated Diffusion Facilitated diffusion (or facilitated transport) is a process of diffusion, facilitated by **transport proteins**. In facilitated diffusion, substances must bind to specific proteins to cross a cellular membrane. They are specific transmembrane transport proteins. These integral proteins are sometimes known as **gateway proteins**. They act as carriers or pores. Facilitated diffusion may occur either across biological membranes or through aqueous compartments.

These proteins have specific binding sites for substances to be brought into the cell, through channels. Those substances, which cannot diffuse through the semipermeable membrane without help, are transported by facilitated diffusion. One site is specific for one substance.

Large molecules like glucose, certain amino acids and vitamins are carried through this way. The number of binding sites is limited. Related substances could compete for the same carrier or pore. Under both these situations, facilitated diffusion gets reduced. Also when a substance reaches high concentrations due to lack of available protein, facilitated diffusion stops due to saturation.

2. Primary Active Transport

Primary active transport, also called **direct active transport**, directly uses energy to transport molecules across a membrane, usually in the form of ATP. Cellular energy is used to drive the substance uphill against its concentration, pressure or electrical gradient. Transport of substances could be in either direction.

Examples include transport of large molecules (nonlipid soluble) and the sodium–potassium pump. It is carried out in nearly every cell in the body.

Na–K ATPase is the enzyme which acts as the carrier. It pumps 3 Na ions out in exchange for 2 K ions pumped in. Thus, homeostasis is maintained, as excess Na^+ is pumped out in exchange for K^+.

Other pumps include the Ca-ATPase, and the H-ATPase.

These ATPase pumps help in maintaining the normal ionic concentration, which is necessary for normal intracellular activities to be carried out.

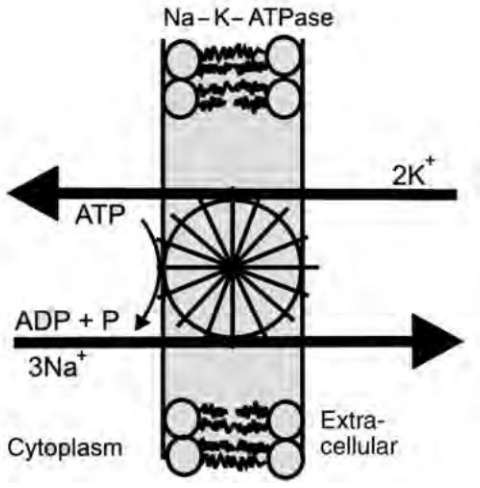


Fig. 2.6 *Primary active transport*

Different concentrations of Na^+ and K^+ in cytosol and extracellular fluid are necessary for maintaining normal cell volume (cells neither shrink nor swell due to the Na–K pump because of movement of water by osmosis out of/into the cell) and for the ability of some cells to generate electrical signals like action potentials.

3. Secondary Active Transport

Here, proteins similar to those for facilitated diffusion are used. The gradient for one molecule can cause the other to move against its own diffusion gradient.

Normal active transport (Na–K ATPase) makes a strong Na gradient, which in turn powers many secondary-active-transport mechanisms, e.g., Na–Glucose co-transport.

In secondary active transport, in contrast to primary active transport, there is no direct coupling of ATP; instead, the electrochemical potential difference created by pumping ions out of the cell is used.

A transport protein, simultaneously binds to Na^+ and another substance and there is change in shape. Both substances cross the membrane at the same time. These transporters which move two substances in the same direction are called **symporters**.

An example is the glucose symporter SGLT1, which co-transports one glucose (or galactose) molecule into the cell for every two sodium ions it imports into the cell. This symporter is located in the small intestines, trachea, heart, brain, testes, and prostate. It is also located in the S3 segment of the proximal tubule in each nephron in the kidneys:

In **antiport**, two species of ions or other solutes are pumped in opposite directions across a membrane. One of these is allowed to flow from high to low concentration which yields the entropic energy to transport the other solute from a low-concentration region to a high one.

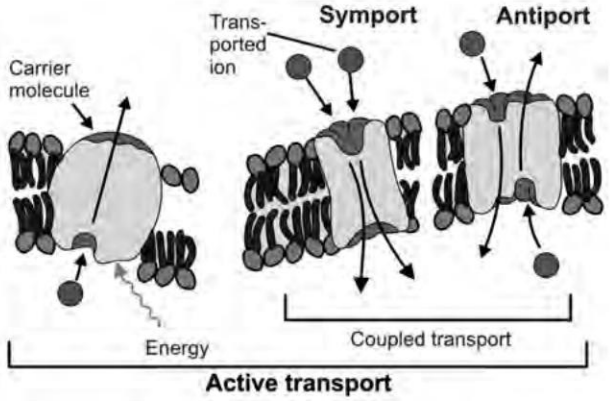


Fig. 2.7 *Secondary active transport*

An example is the sodium–calcium exchanger or antiporter, which allows three sodium ions into the cell to transport one calcium ion out. These transporters are called **antiporters**.

4. Vesicle Mediated Transport

Another process of transport involving the formation and movement of membrane-bound vesicles is called **vesicle mediated transport.**

Vesicles and vacuoles that fuse with the cell membrane may be utilized to release or transport chemicals out of the cell or to allow them to enter a cell. Both the processes require energy supplied by ATP. Hence, transport in vesicles is an active process. It is of two types:

- Endocytosis
- Exocytosis

(a) Endocytosis Endocytosis is a process in which a substance enters the cell without passing through the cell membrane. This process is subdivided into three different types:

- Pinocytosis
- Phagocytosis
- Receptor-mediated endocytosis

Pinocytosis This process is concerned with the uptake of solutes and single molecules such as proteins. The cell could also engulf nonspecific or unwanted particles.

The plasma membrane forms an invagination and a vesicle, and any substance found within the area of invagination is brought into the cell.

The vesicle detaches from the plasma membrane and enters into the cytosol. The vesicle, then fuses with the lysosome, and enzymes degrade the material. This material gets dissolved in water, and hence this process is also called **cellular drinking**. Materials dissolved in liquids are ingested by the cell in this way. This material is relatively small.

Pinocytosis occurs in almost all cells and occurs continuously.

Phagocytosis Phagocytosis occurs only in certain specialized cells like neutrophils, monocytes and macrophages. It occurs sporadically. This process is seen in which the cell engulfs large solid particles such as bacteria, virus and worn-out cells.

In this process, the cell changes shape. The phagocytic cell gets attracted to a particle like a bacteria or virus by chemical substances. This is called **chemotaxis**. The cell then sends out membrane projections called **pseudopodia**, or false feet. Some interaction occurs between the surface of the phagocytic cell and the particle that is ingested. The pseudopodia then surround the particle and the plasma membrane of the projections fuse to form a vesicle. This vesicle is known as **phagosome**, which now enters the cytoplasm. The phagosome fuses with the lysosome, and lysosomal enzymes break the ingested material. The undigested material is also called **residual body**. This procedure is also called **cellular eating**.

The process of phagocytosis is a protective mechanism and helps fight disease. Macrophages help dispose the invading microbes and the worn-out red blood cells. Neutrophils are helpful in removing the invading microbes. In an infected wound, the mixture of dead neutrophils, macrophages and the body cells is called **pus**.

Receptor-mediated endocytosis Receptor-Mediated Endocytosis (RME), also called clathrin-dependent endocytosis, is a process by which specific molecules are ingested into the cells by the inward budding of plasma membrane. Vesicles contain a specific binding protein in the cell membrane called a **receptor**, through which a receptor–ligand interaction takes place.

After the binding of a ligand to plasma membrane receptors, a signal is sent through the membrane. A protein called **clathrin** attaches to the membrane on its cytoplasmic side. Many clathrin molecules come together to form a basketlike structure, which wraps around the receptor–particle complex and this causes the membrane to invaginate. The edges of the membrane around the receptor–particle complex fuse and a part gets detached, forming a vesicle called the clathrin-coated vesicle. Almost immediately, the clathrin-coated vesicle uncoats. The uncoated vesicle fuses with a vesicle known as **endosome**. The particles separate from the receptor in the endosome.

For example, LDL particles detach from the endosome and fuse with lysosome, containing digestive enzymes. Larger particles are broken into smaller particles which leave the lysosome and are ready for use, i.e., fatty acids and amino aclds can be used for ATP production. Cholesterol can be used for synthesis of steroids like estrogen.

Since the receptor is internalized with the ligand, the system is saturable and uptake will decline until receptors are recycled to the surface.

The receptors lie in the elongated process of the endosome and get pinched off. The receptors return to the plasma membrane and can be used again.

The ligands which enter by receptor-mediated endocytosis are hormones, growth factors, toxins, lectins, serum-transport proteins and antibodies.

(b) Exocytosis Exocytosis is the opposite of endocytosis. The initial process in exocytosis is the binding of a membrane protein protruding from the cytoplasmic side of the vesicle with a membrane protein on the cytoplasmic side of the target site on the plasma membrane. The phospholipid regions of the two membranes merge, and an opening to the outside of the cell develops. The contents of the vesicle are released to the environment, and the vesicle membrane is smoothly incorporated into the plasma membrane.

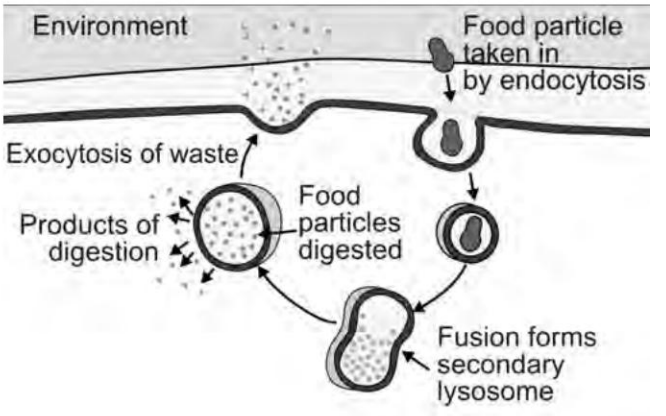


Fig. 2.8 *Exocytosis*

Secretion of proteins like enzymes, peptide hormones and antibodies from cells are examples of exocytosis. Release of neurotransmitters from presynaptic neurons also occurs by exocytosis.

In **transcytosis**, vesicles undergoing endocytosis on one side of the cell move across the cell and those under exocytosis, on the other side. The best example of transcytosis is the movement of antibodies across the placenta in pregnant women into the fetal circulation.

2.1.4 Ion Channels

Ion channels regulate the flow of ions across the membrane in all cells. They are integral membrane proteins; or an assembly of several proteins. Such multi-sub-unit assemblies usually involve a circular arrangement of homologous proteins, closely packed around a water-filled pore, through the plane of the membrane or lipid bilayer.

In ion channels, passage through the pore is governed by a 'gate,' which may be opened or closed by chemical or

electrical signals, temperature or mechanical force, depending on the type of the channel—sodium, potassium and calcium channels.

Ion channels may be classified by gating, i.e., what opens and closes the channels.

Voltage-gated ion channels open or close depending on the voltage gradient across the plasma membrane.

For most voltage-gated ion channels, the pore-forming sub-unit(s) are called the α sub-unit, while the auxiliary sub-units are denoted β, γ, and so on.

Ligand-gated ion channels open or close depending on the binding of ligands to the channel.

Ligand-gated ion channels, also known as **ionotropic receptors**, open in response to specific ligand molecules binding to the extracellular domain of the receptor protein. Ligand binding causes a change in the structure of the channel protein that ultimately leads to the opening of the channel gate and subsequent ion flux across the plasma membrane.

The **archetypal channel** pore is just one or two atoms wide at its narrowest point and is selective for specific ions, such as sodium or potassium. These ions move through the channel pore in single file, nearly as quickly as the ions move through free fluid.

In so-called 'excitable' cells like neurons and muscle cells, some channels open or close in response to changes in the charge, i.e., positive (cation) or negative (anion) across the plasma membrane, e.g., an impulse passes down a neuron, and the reduction in the voltage opens sodium channels in the adjacent portion of the membrane. This allows the influx of Na^+ into the neuron and thus the nerve impulse continues to propagate. Some 7000 sodium ions pass through each channel during the brief period (about 1 millisecond) while it remains open.

Metal ions, such as Na^+, K^+, Mg^{++}, or Ca^{++}, require ion pumps or ion channels to cross membranes and distribute through the body.

The cytosol contains a concentration of potassium ions (K^+) as much as 20 times higher than that in the extracellular fluid. Conversely, the extracellular fluid contains a concentration of sodium ions (Na^+) as much as 10 times greater than that within the cell.

These concentration gradients are established by the active transport of both ions. And, in fact, the same transporter, called the Na^+/K^+ ATPase, does both jobs. It uses the energy from the hydrolysis of ATP to actively transport 3 Na^+ ions out of the cell for each 2 K^+ ions pumped into the cell.

A Ca^{++} ATPase is located in the plasma membrane. It uses the energy provided by one molecule of ATP to pump one Ca^{++} ion out of the cell. The activity of these pumps helps maintain the ~20,000-fold concentration gradient of Ca^{++} between the cytosol and the extracellular fluid.

In a resting skeletal muscle, there is a much higher concentration of calcium ions (Ca^{++}) in the sarcoplasmic reticulum than in the cytosol. Activation of the muscle fiber allows some of this Ca^{++} to pass by facilitated diffusion into the cytosol where it triggers contraction.

After contraction, this Ca^{++} is pumped back into the sarcoplasmic reticulum. This is done by another Ca^{++} ATPase that uses the energy from each molecule of ATP to pump 2 Ca^{++} ions.

1. Sodium-channel Blocker

Sodium-channel blockers (SCBs) are agents that impair conduction of sodium ions (Na^+) through sodium channels.

They act, both, at extra and intracellular levels. Their role at the intracellular level is utilized in clinical practice. Drugs block sodium channels by blocking from the intracellular side of the channel.

They are

- Local anesthetics
- Class I antiarrhythmic agents—Class I agents, also called membrane-stabilizing agents, interfere with the (Na^+) channel, and are grouped by their effect on the Na^+ channel, and by their effect on cardiac action potentials
- Some anticonvulsants

2. Potassium-channel Blocker

Potassium-channel blockers (PCBs) comprise Class III antiarrhythmic compounds. These drugs bind to and block the potassium channels that are responsible for Phase 3 repolarization. Therefore, blocking these channels slows (delays) repolarization, which leads to an increase in action potential duration and an increase in the Effective Refractory Period (ERP). By increasing the ERP, these drugs are very useful in suppressing tachyarrhythmias caused by mechanisms. These drugs are Amiodorone, Dronedorone, and Sotalol.

3. Calcium-channel Blocker

Calcium-channel blockers (CCBs) are a class of drugs and natural substances that disrupt the calcium (Ca^{++}) conduction of calcium channels.

Calcium-channel blockers work by blocking Voltage-Gated Calcium Channels (VGCCs) on many excitable cells of the body such as cardiac muscles, smooth muscles of blood vessels, or neurons.

In the heart, a decrease in calcium available for each beat results in a decrease in cardiac contractility.

In blood vessels, a decrease in calcium results in less contraction of the vascular smooth muscle and therefore an increase in arterial diameter—a phenomenon called **vasodilation**. (CCBs do not work on venous smooth muscle).

Vasodilation decreases total peripheral resistance, while a decrease in cardiac contractility decreases cardiac output. Since blood pressure is determined by cardiac output and peripheral resistance, blood pressure drops.

The main clinical usage of calcium-channel blockers is to decrease blood pressure. It is for this action that they are used in individuals with hypertension.

Most calcium-channel blockers decrease the force of contraction of the myocardium. This is known as the **negative inotropic effect** of calcium-channel blockers (hence not used in individuals with cardiomyopathy).

Some calcium-channel blockers also slow down the conduction of electrical activity within the heart by blocking the calcium channel during the plateau phase of the action potential of the heart (see cardiac action potential). This results in a negative chronotropic effect resulting in a lowering of the heart rate. The negative chronotropic effects of calcium-channel blockers make them a commonly used class of agents in individuals with atrial fibrillation or flutter, in whom control of the heart rate is necessary.

There are different classes of calcium-channel blockers.

- **Dihydropyridine** calcium-channel blockers are often used to reduce systemic vascular resistance and arterial pressure, but are not used to treat angina, because the vasodilation and hypotension can lead to reflex tachycardia. They are Amlodipine, Cilnidipine, Felodipine, Nicardipine, Nifedipine, etc.
- **Phenylalkylamine** calcium-channel blockers are relatively selective for myocardium. They reduce myocardial oxygen demand and reverse coronary vasospasm, and are often used to treat angina. They have minimal vasodilatory effects compared with dihydropyridines. Action is intracellular, mainly due to negative inotropic effect, e.g., Verapamil.
- **Benzothiazepine** calcium-channel blockers are an intermediate class between phenylalkylamine and dihydropyridines in their selectivity for vascular calcium channels. By having both cardiac depressant and vasodilator actions, benzothiazepines are able to reduce arterial pressure without producing the same degree of reflex cardiac stimulation caused by dihydropyridines, e.g., Diltiazem.

2.2 NUCLEUS AND GENETIC MATERIAL

Every cell in the body has a nucleus with the exception of mature erythrocytes. The nucleus is the largest organelle. The cells with nuclei are called **eukaryotes** and those without nuclei are called **prokaryotes**.

Most cells have one nucleus and are called **uninucleated cells**, while some cells are **multinucleated**, e.g., skeletal muscle cells.

The nucleus is situated near the center of the cell and is spherical in shape.

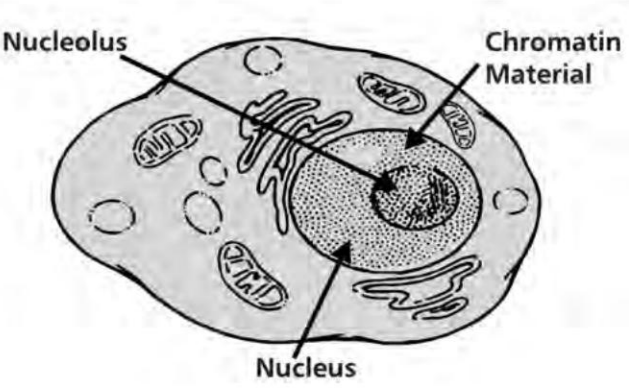


Fig. 2.9 *Location of the nucleus*

2.2.1 Structure

The nucleus consists of nuclear membrane, nucleoplasm and nucleolus.

1. Nuclear Membrane

The nuclear membrane is a double-layered membrane. The outer layer is continuous with the endoplasmic reticulum, and the lumen is continuous with the lumen of the endoplasmic reticulum.

There are pores in the nuclear membrane which allow materials to be exchanged between the nucleoplasm and cytoplasm.

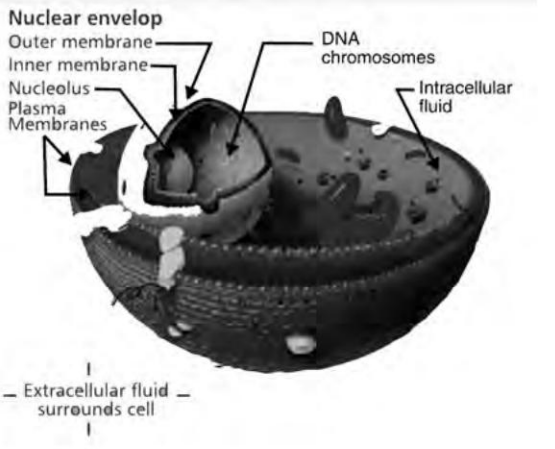


Fig. 2.10 *Structures of the nucleus*

2. Nucleoplasm

The nucleoplasm is a gel-like ground substance of the nucleus and contains the genetic material.

3. Nucleoli

There are one or more nucleoli. The nucleolus contains Ribo-Nucleic Acid (RNA) and some proteins.

4. Genetic Material (GM)

The nucleus contains the body's genetic material which directs the activity of the cell.

This is built from Deoxy ribo Nucleic Acid (DNA) and proteins called **histones**, which are coiled together forming a fine network of threads called **chromatin**. Chromatin is like a string of beads. During cell division, the chromatin replicates and becomes more tightly coiled, forming chromosomes.

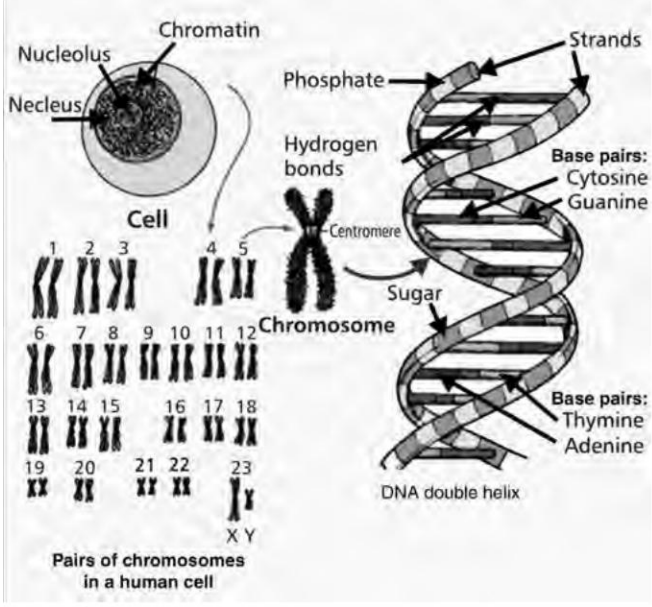


Fig. 2.11 *Structure of the genetic material*

The functional sub-units of chromosomes are called **genes**. Each cell contains the total complement of genes required to synthesize all the proteins in the body.

The RNA in the nucleolus is synthesized by five different pairs of chromosomes and stored in the nucleolus. Later, it is condensed to form the sub-units of ribosome. All the sub-units are transported to the cytoplasm via the pores on the nuclear membrane. Ribosomes are formed by the fusion of these sub-units, which play an important role in the formation of proteins.

The genetic information of an organism is stored in the form of DNA, which forms the gene. DNA forms the chemical basis of hereditary characters. It also acts as the carrier of genetic information. It contains instructions for the synthesis of proteins in the ribosome.

A gene is a portion of a DNA molecule. It has a very specific property—that of synthesizing a specific protein from amino acids. Three successive pairs are called **triplets** and the arrangement of the triplets along the portion of DNA is known as gene.

RNA is formed from DNA and is present in the cytoplasm of the cell. RNA carries out the various functions coded in the genes.

2.2.2 Functions

1. The nucleus controls all the activities of the cell.
2. Genes control cell division.
3. Hereditary information is stored in the genes and transformed from one generation to another.
4. Specific enzymes responsible for various metabolic reactions in the cell, function due to the genetic information provided by the DNA present in the nucleus.

2.3 CYTOPLASM

Cytoplasm is the simplest structure of the cell. Organelle-free sap is called cytosol, and there is no specific structure of cytosol. It has particles of different shapes and sizes and these particles are proteins, carbohydrates, lipids or electrolytes in nature. Organelles which vary in structure and function are also present in the cytoplasm.

The cytoplasm consists of two zones:

1. Endoplasm
2. Ectoplasm

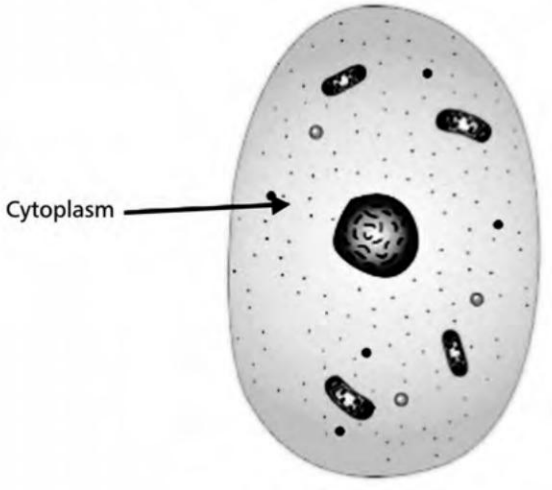


Fig. 2.12 *Cytoplasm*

Endoplasm is fluid like and interposed between the nucleus and ectoplasm.

Ectoplasm lies just beneath the cell membrane and consists of a network of microfilaments. Microfilaments are chiefly active filaments and support the cell membrane.

2.3.1 Cell Organelles

Cells contain some common structures which carry out specific cellular processes.

There are two types of organelles.

I. Organelles Bound by Limiting Membrane

- Endoplasmic reticulum
- Golgi apparatus
- Lysosome
- Peroxisome
- Secretory vesicles
- Mitochondria

II. Organelles not Bound by Limiting Membrane

- Chromosomes—centrioles and centrosomes
- Ribosomes
- Cytoskeleton—microfilaments—microtubules and microtrabeculae

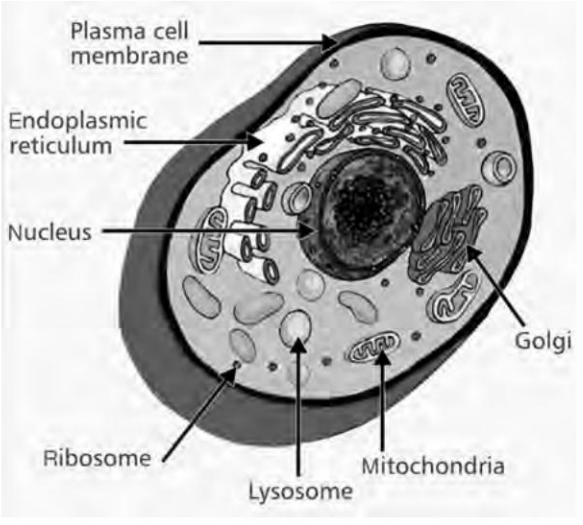


Fig. 2.13 *Cell organelles*

1. Endoplasmic Reticulum (ER)

There are several membrane complexes, formed by lipid and proteins, which are interconnected by separate organelles. They vary in shape, size and amount. There is a limiting membrane.

The endoplasmic reticulum extends from the cell membrane, coats the nucleus, surrounds the mitochondria and appears to connect directly to the Golgi apparatus. It gives a railway-track appearance.

The lumen of the endoplasmic reticulum contains a fluid called **endoplasmic matrix**.

There are two kinds of endoplasmic reticulum:

- Rough endoplasmic reticulum
- Smooth endoplasmic reticulum

(a) Rough Endoplasmic Reticulum Rough endoplasmic reticulum is known as **ergastoplasm**. Granular ribosomes are attached to it. It synthesizes membrane lipids and secretory proteins and is transported through the cell. (See Fig. 2.14)

(b) Smooth Endoplasmic Reticulum Smooth endoplasmic reticulum does not have attached ribosomes. Many enzymes are present on the outer surface of this part of the reticulum. These enzymes are concerned with various metabolic processes of the cell. (See Fig. 2.15)

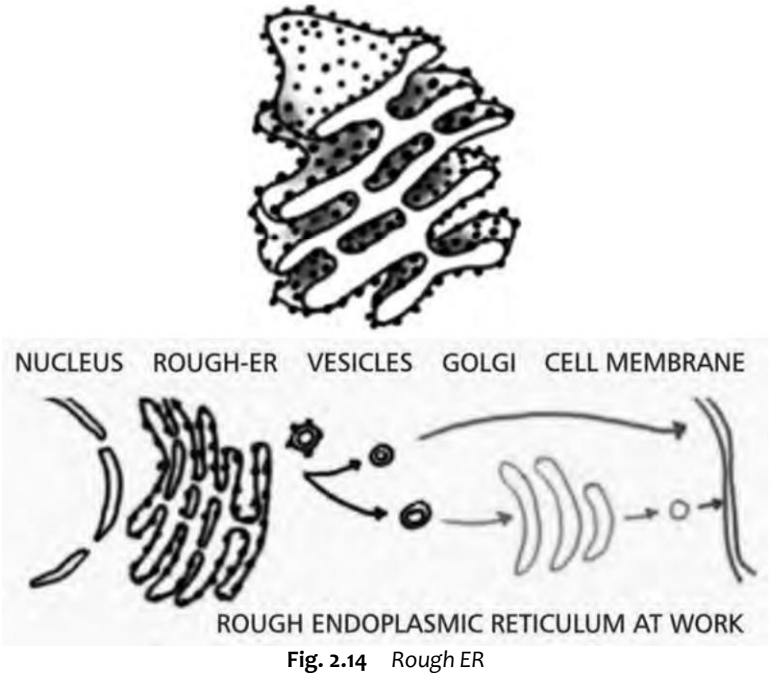


Fig. 2.14 *Rough ER*

Fig. 2.15 *Smooth ER*

They are involved in
- Lipid synthesis
- Synthesis of nonprotein substances like steroid hormones, cholesterol, etc.
- Catabolism of toxic substances like carcinogens
- Modification and transport of proteins synthesized in the rough endoplasmic reticulum

2. Golgi Apparatus

The Golgi apparatus is also known as **Golgi body** or **Golgi complex** or **dictyosomes**. It is present in all the cells except the red blood cells. There is a unique stack of smooth surfaced compartments that make up the Golgi complex. Each Golgi apparatus consists of 5 to 8 membranous sacs. The sacs are flattened and called **cisternae**. It has a proximal or cis compartment, medial compartment and a distal or trans compartment.

Fig. 2.16 *Golgi apparatus*

Functions

The processing and delivery of protein molecules to different parts of the cell is the main function. The proteins synthesized in the endoplasmic reticulum are transported to the Golgi apparatus in the form of reticular vesicles, where they are processed, sorted out and packed in the form of secretory granules, secretory vesicles, lysosomes, etc. These secretory vesicles move towards the plasma membrane where the contents may be expelled by exocytosis.

3. Lysosomes

Lysosomes are situated throughout the cytoplasm. Lysosomes have the thickest covering membrane. They contain a packet of enzymes which can digest proteins, lipids, carbohydrates and nucleic acids. Together, all the enzymes are called lysozymes.

They are synthesized in the rough endoplasmic reticulum. They are then processed and packed into lysosomal vesicles in the Golgi apparatus.

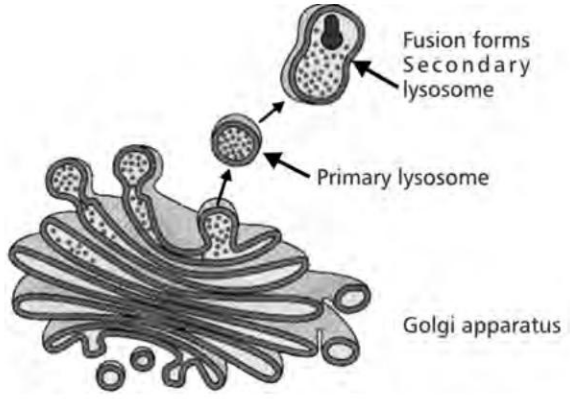


Fig. 2.17 *Lysosome*

As long as the membrane is intact, the enzymes act locally; but when bacteria or foreign bodies enter the cell, the membrane ruptures and the enzymes are released into the cytoplasm and they digest the bacteria or foreign particles.

4. Peroxisomes

Peroxisomes are small organelles, also called **micro bodies**. Peroxisomes are derived from the endoplasmic reticulum. They contain oxidative enzymes.

Fig. 2.18 *Peroxisomes*

Functions

1. They carry out oxidative reactions in which toxic hydrogen peroxide is produced and is destroyed by the enzyme catalase.
2. The oxidative enzymes also destroy other enzymes necessary for the production of hydrogen peroxide. Thus, peroxisomes are involved in the detoxification of peroxide.
3. They are also concerned with gluconeogenesis from fats.

5. Secretory Vesicles

Secretory vesicles are formed in the endoplasmic reticulum and processed and packed in the Golgi apparatus.

6. Mitochondria

Mitochondria are very small rod-shaped organelles of up to 0.5 to 10 micrometers in diameter. Their shape is not static

and they assume different shapes under different metabolic conditions. Mitochondria are the powerhouse of the cell. They act like the digestive system, take in nutrients, break them down, and create energy for the cell. The process of creating cell energy is known as **cellular respiration**. Most of the chemical reactions involved in cellular respiration happen in the mitochondria.

They convert oxygen and nutrients into Adenosine TriPhosphate (ATP). ATP is the chemical energy of the cell that powers the cell's metabolic activities. This process is called **aerobic respiration** and that is the reason why animals breathe in oxygen. Without mitochondria, their cells would only be able to obtain energy from **anaerobic respiration**, a process much less efficient than aerobic respiration, and hence their existence would not be possible. Mitochondria enable cells to produce 15 times more ATP than they could otherwise, and humans need large amounts of energy in order to survive.

The number of mitochondria present in a cell depends upon the metabolic requirements of that cell, and may range from a single large mitochondrion to thousands. Fewer mitochondria are seen in the cell if the purpose of the cell is to transmit nerve impulses, while in a muscle cell more of them are seen, as it needs loads of energy. If the cell experiences lack of energy, more mitochondria can be created. Unusually, mature erythrocytes have no mitochondria at all.

Mitochondria have been implicated in several human diseases, including mitochondrial disorders and cardiac dysfunction.

Structure Mitochondria are composed of compartments that carry out specialized functions. These compartments or regions include the outer membrane, the intermembrane space, the inner membrane, and the cristae and matrix.

The outer mitochondrial membrane encloses the entire organelle. It has a protein-to-phospholipids ratio similar to that of the eukaryotic plasma membrane. It contains large numbers of integral proteins called **porins**.

The intermembrane space is the space between the outer membrane and the inner membrane. The outer membrane is freely permeable to small molecules, and so the concentrations of small molecules such as ions and sugars in the intermembrane space are the same as the cytosol.

The inner mitochondrial membrane is folded into numerous cristae, which expand its surface area enhancing its ability to produce ATP. For typical liver mitochondria, the area of the inner membrane is about five times greater than the outer membrane. Where there is a greater demand for ATP, such as muscle cells, there are even more cristae. These folds are studded with small round bodies known as F1 particles or oxysomes. These folds are actually invaginations of the inner membrane, which can affect overall function.

It contains more than 100 different polypeptides and has a very high protein-to-phospholipid ratio. Around 1/5 of the total protein in a mitochondrion is found in the inner membrane. It is also rich in an unusual phospholipid, **cardiolipin**.

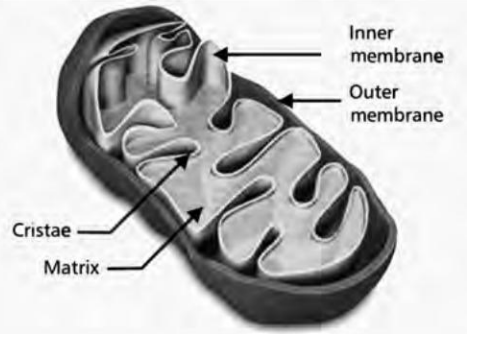


Fig. 2.19 *Mitochondrion—immer structure*

Both the membranes are covered with thousands of small particles which are thought to be enzymes.

The matrix is the space enclosed by the inner membrane. It contains about 2/3 of the total protein found in a mitochondrion. The matrix is important in the production of ATP and does this with the help of **ATP synthase**, contained in the inner membrane. It is filled with fluid and contains a highly concentrated mixture of hundreds of enzymes, special mitochondrial ribosome, tRNA, and several copies of the mitochondrial DNA genome. Thus modulation of DNA–RNA genes and their replication helps in the study of genetics.

Mitochondrial proteins vary depending on the type of tissue. In humans, 615 distinct types of proteins have been identified from cardiac mitochondria.

Functions

The main function is aerobic respiration.

1. Catabolism of digested food particles—proteins, lipids and carbohydrates—carried out by mitochondria leads to energy production. This energy is stored in the form of chemical energy, bound to ATP molecules. The ATP molecules are broken and energy is released, whenever it is needed. Hence, the mitochondrion is called the powerhouse of the cell.
2. The mitochondria contain enzymes responsible for citric-acid cycle; oxidative phosphorylation and synthesis of ATP.
3. In addition to supplying cellular energy, mitochondria are involved in a range of other processes, such as signaling, cellular differentiation, cell growth, cell death and the control of the cell cycle. It may play a role in the aging process.
4. The modulation of DNA–RNA genes and its replication helps in the study of genetics.

7. Microsomes

In cell biology, microsomes are vesicle-like artifacts, formed from the Endoplasmic Reticulum (ER) when eukaryotic cells are broken up in the laboratory.

Microsomes are a valuable tool for investigating the metabolism of compounds (enzyme inhibition, clearance and metabolite identification) and for examining drug–drug interactions by in-vitro research. Researchers often select microsome lots, based on the enzyme activity level of specific cytochrome P450 (CYP). Some are available to study specific populations (for example, lung microsomes from smokers or nonsmokers). Some are used to meet target CYP activity levels for inhibition and metabolism studies.

Microsomes can be concentrated and separated from other cellular debris by **differential centrifugation**. Unbroken cells, nuclei, and mitochondria sediment separate out at 10,000*g*; whereas soluble enzyme and fragmented ER, which contains cytochrome P450, remain in solution (*g* is the earth's gravitational acceleration). At 100,000*g*, achieved by faster centrifuge rotation, ER sediments out of solution but the soluble enzymes remain in the supernatant. In this way, cytochrome P450 in microsomes is concentrated and isolated. Microsomes have a reddish-brown color, due to the presence of the iron-containing co-factor, heme (haem), in the P450s. P450s are highly abundant in the liver.

8. Centrosomes and Centrioles

The centrosome is situated near the center of the cell. It has two structures called centrioles. Centrioles are cylindrical in shape. During cell division, it is responsible for the movement of chromosomes.

Fig. 2.20 *Centrioles*

9. Ribosomes

Ribosomes are granular structures containing 65% RNA and 35% proteins.

Some ribosomes are free in the cytoplasm, while some are attached to the rough endoplasmic reticulum. (See Fig. 2.21)

Functions Ribosomes are concerned with the synthesis of proteins. (See Fig. 2.21)

10. Cytoskeleton

The cytoskeleton contains a network of fine structures called **microtubules**, **microfilaments** and **microtrabeculae**. The shape of the cell is determined by the cytoskeleton. It also

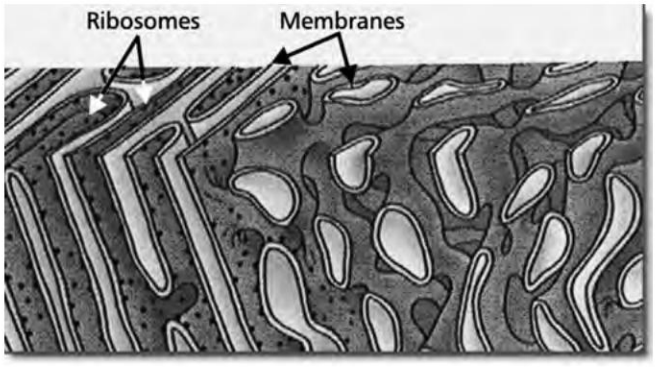


Fig. 2.21 *Ribosomes*

helps in the movements of the cell. The response of the cell to external stimuli is guided by the cytoskeleton.

(a) Microtubules Microtubules are long, unbranched slender, cylindrical structures with an average diameter of 25 nm. Tubulin, molecules of protein present in microtubules, are arranged in bundles which give structural strength to the cell.

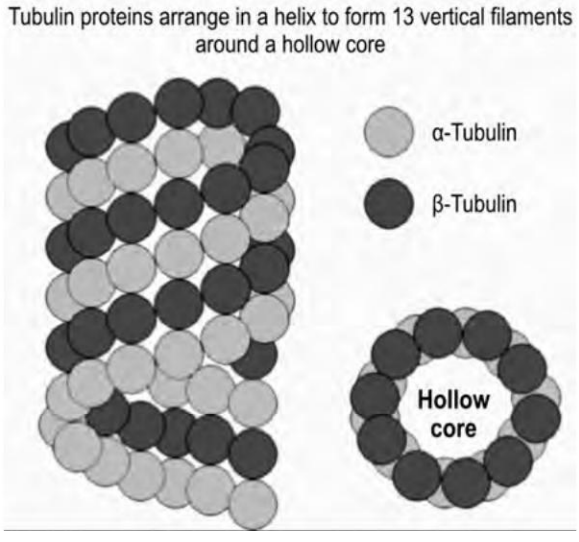


Fig. 2.22 *Microtubules*

Functions

1. An important function is their role in assembly and disassembly of spindle structures during mitosis.
2. They form the transport system of the cell.
3. They provide internal structure to the cell.

(b) Microfilaments Microfilaments are present in the cell and are long nontubular organelles. They contain contractile proteins called **actin** and **myosin**. Microfilaments of the ectoplasm contain only actin molecules, and those present in the endoplasm contain both actin and myosin molecules. (See Fig. 2.23)

Fig. 2.23 *Microfilaments*

Functions

1. The microfilaments give structural strength to the cell.
2. They are responsible for the shape of the cell.
3. They may be involved in the generation of forces for internal cell motion.

(c) Microtrabeculae They appear to be very fragile tubes that form a transient network in the cytosol.

Functions Probably they form unstable multienzyme complexes.

2.4 CELL CYCLE

In cell cycle, a series of events take place in a cell, leading to its replication.

In prokaryotes, the cell cycle occurs via a process termed **binary fission**.

Human cells contain 23 pairs of chromosomes. One member of each pair is inherited from each parent. The two chromosomes making a pair are called **homologous chromosomes**. There is one pair of chromosomes called **sex chromosomes**, designated X and Y. In males, the sex chromosomes are X and Y; while in females, they are X and X. Somatic cells have two sets of chromosomes and hence are called **diploid cells**.

During development from stem to fully differentiated cells in the body, the cells divide (mitosis) and there is another phase where they appear to be resting (interphase). This sequence of activities exhibited by cells is called the **cell cycle**.

The cell-division cycle is a vital process by which a single-celled fertilized egg develops into a mature organism, as well as the process by which hair, skin, blood cells and some internal organs are renewed.

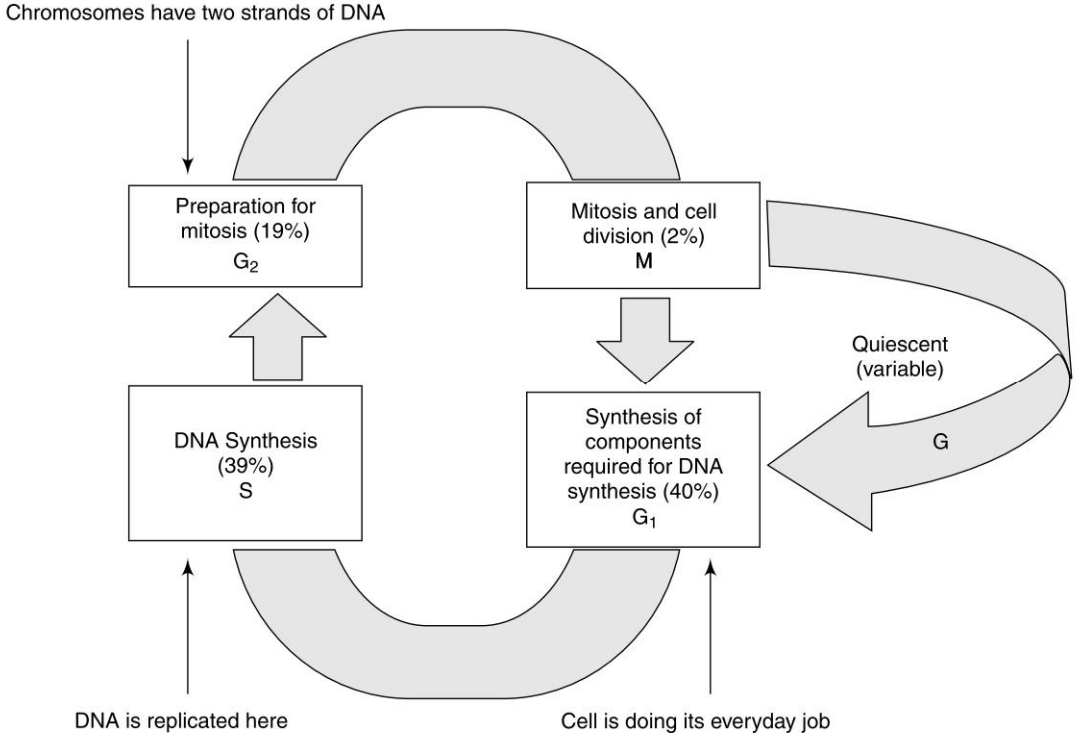


Fig. 2.24 *Cell cycle*

The whole cycle can be divided into two parts:

- Interphase
- Cell division

2.4.1 Interphase

Interphase lasts at least 12 to 24 hours, but is variable, and depends on the size of the cell. Here, the cell is constantly synthesizing RNA, producing protein and growing in size. Interphase can be divided into stages:

1. Gap 1 or G1 Phase

Cells increase in size and produce RNA and synthesize protein. In this phase, the cell is metabolically active. The mechanism activated during this period ensures that everything is ready for DNA synthesis. At this time, each of the two chromosomes have just one molecule of DNA. Chromosomes with one strand of DNA are called unduplicated or unreplicated chromosomes. There is also replication of most of the organelles and cytosolic components. This phase lasts 8 to 10 hours.

2. S Phase

The DNA replicates or duplicates. The chromosomes will now have two molecules of DNA and are called duplicated or replicated chromosomes. The two identical cells will have same genetic material. This phase lasts 8 hours.

3. G2 Phase

The cell is carrying out processes necessary for mitosis to begin. Enzymes and other proteins necessary for cell division are synthesized.

When there is replication of DNA, the helical structure partly uncoils and separates at the point where the hydrogen bonds connect base pairs. They, then, pair with the complementary base of a newly synthesized nucleotide. Chemical bonds form between neighboring nucleotides. This process goes on till each of the original DNA joins the newly formed complementary DNA strand.

Many times a cell will leave the cell cycle, temporarily or permanently. It exits the cycle at G_1 and enters a stage designated G_0 (G zero). A G_0 cell is often called 'quiescent'. Often G_0 cells are terminally differentiated. They will never re-enter the cell cycle but instead will carry out their function in the organism until they die.

For other cells, G_0 can be followed by re-entry into the cell cycle. Most of the lymphocytes in human blood are in G_0. However, with proper stimulation, such as encountering the appropriate antigen, they can be stimulated to re-enter the cell cycle (at G_1) and proceed on to new rounds of alternating **S phases** and **mitosis**.

2.4.2 Cell Division

Cells are constantly sloughed off, dying and being replaced by new ones in the body. When damaged tissues are repaired, the new cells must be exact copies of the cells being replaced, so as to retain normal function of cells.

Cell division is a process by which a cell, called the **parent cell**, divides into two or more cells, called **daughter cells**. Each new cell has exactly the same genetic material (DNA) as the cell that produced it. There are two types of cell division:

1. Mitosis
2. Meiosis

1. Mitosis

It is the process in which a cell separates the chromosomes in its cell nucleus, into two identical sets in two daughter nuclei. It is followed immediately by **cytokinesis**, which divides the nuclei, cytoplasm, organelles and cell membrane into two daughter cells, containing equal shares of these cellular components.

For convenience, cell division is divided into four phases—prophase, metaphase, anaphase and telephase. As such, cell division is a continuous process where one phase merges with the next.

(a) Prophase In this phase, the chromatin condenses into chromosomes. Each chromosome has a centromere and four chromatids attached to it. DNA forms a duplicate of itself.

The nuclear covering breaks down and nuclear membrane slowly disappears. The two identical sets of chromatids move to opposite poles, and are held together by fibrils which form spindles so that thin spindles extend from pole to pole. The nucleolus disappears.

In mitosis, chromosomes are independent and divide into two daughter chromosomes, while in meiosis, the chromosomes of homologous pairs form a unit and mix with each other.

(b) Metaphase Spindle fibers align the chromatids along the middle of the cell nucleus. This line is referred to as the metaphase plate. This organization helps to ensure that in the next phase, when the chromatids are separated, each new nucleus will receive one copy of each chromosome.

In mitosis, one of the two daughter chromosomes move towards each centromere and in meiosis, one of each homologous pair go to opposite centromeres.

(c) Anaphase The centromeres divide. Sister chromatids separate and move toward the corresponding poles. Now, the chromatids are called chromosomes. These chromosomes are pulled by the microtubules, forming a V-shape with the centromere pulling the chromosomes behind it towards the chromosomes.

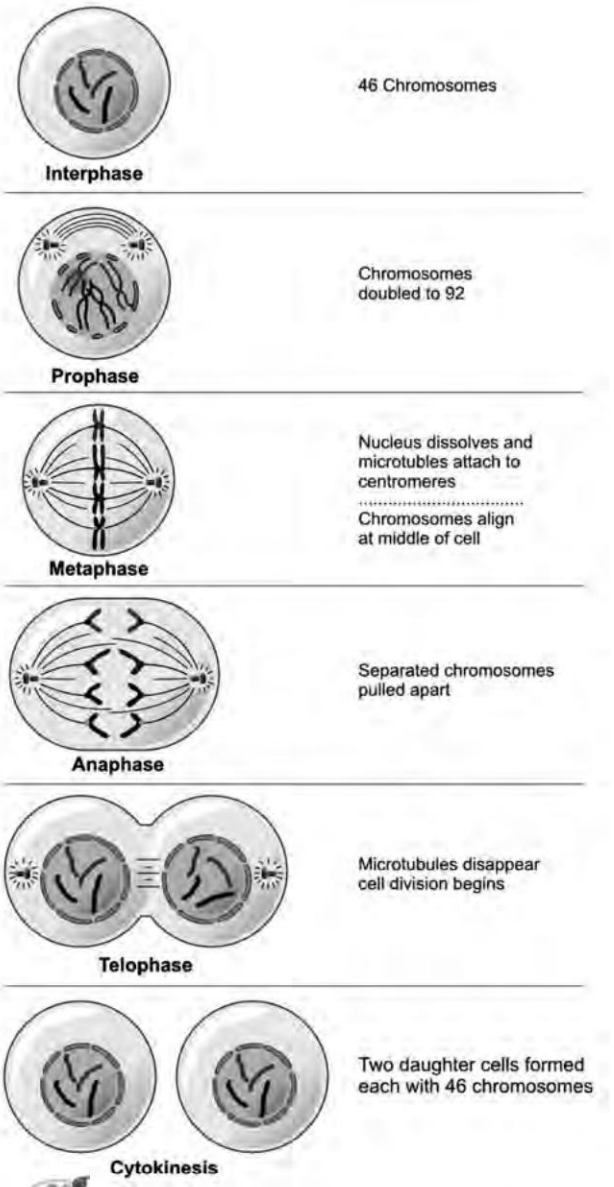


Fig. 2.25 *Mitosis (Refer colour figure)*

(d) Telophase New membranes form around the daughter nuclei. The condensed chromatin expands. The chromosomes uncoil and once again are seen as threadlike chromatin. The nuclear membrane reappears around each chromatin mass. Nucleoli also reappear in the identical nuclei. The spindle fibers disperse, and cytokinesis or the partitioning of the cell may also begin during this stage.

(e) Cytokinesis In this stage, there is division of the cytoplasm and the organelles into two identical cells. It starts in late anaphase and is completed after telophase.

At the center, the cell constricts, divides and two daughter cells are formed with the same number of chromosomes.

At the time of cell division, the organelles in the cytoplasm are incomplete and develop as the cell matures.

In mitosis, each cell formed receives chromosomes that are alike in composition and equal in number to the chromosomes of the parent cell.

2. *Meiosis*

Meiosis is the type of cell division by which germ cells (eggs and sperm) are produced. Meiosis involves a reduction in the amount of genetic material.

The ovum matures in the ovary and the sperm matures in the testes. In meiosis, four daughter cells are produced after two cell divisions, i.e., one parent cell produces four daughter cells. Daughter cells have half the number of chromosomes found in the original parent cell. In human beings, each of the daughter cell has 23 chromosomes called the **haploid number**. When the ovum is fertilized, the zygote that is formed has 46 chromosomes, half from the father and half from the mother.

Sex chromosomes determine the sex of an individual. A woman has two X chromosomes (XX) and a man, one X and one Y (XY). When an X-sperm is combined with an egg,

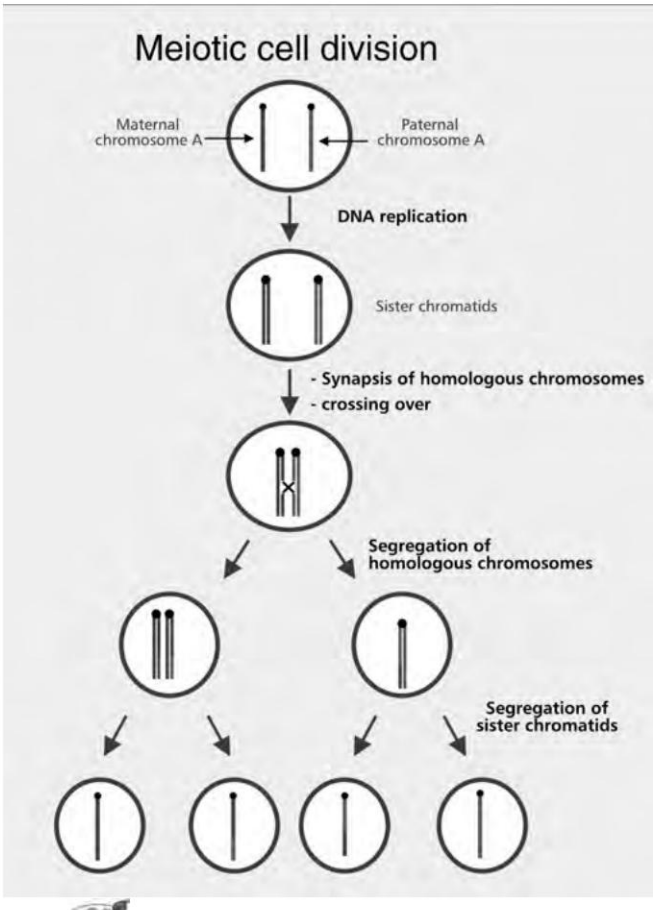


Fig. 2.26 *Meiosis (Refer colour figure)*

the resulting zygote (fertilized egg) will contain two X (XX) chromosomes and the child will be female. Combination of a Y-sperm and an egg will produce a male child (XY).

Meiosis differs from mitosis primarily because there are two cell divisions in meiosis, resulting in cells with a haploid number of chromosomes.

2.4.3 Clinical Significance

Cell division can be affected by acetyl groups acting as molecular switches. These switches may prove to be a crucial factor in the development of new therapies against diseases like cancer, Alzheimer's or Parkinson's.

Sometimes errors may take place during cell division, which is normally corrected by specialized genes. If this correction does not take place then these same genes can lead to the death of the cell, which is called **apoptosis.** If apoptosis is inhibited then uncontrolled cell division takes place which is a distinguishing feature of cancer cells. Here there is formation of a mass of proliferating cells, called a **neoplasm** (new growth). Chemotherapy is used to treat cancer. Some of these drugs stop cell division by inhibiting the formation of spindles. The disadvantage of these drugs is that, they also have this effect on rapidly growing normal cells. This causes side effects like fatigue, nausea, hair loss, diarrhea and decreased resistance to disease.

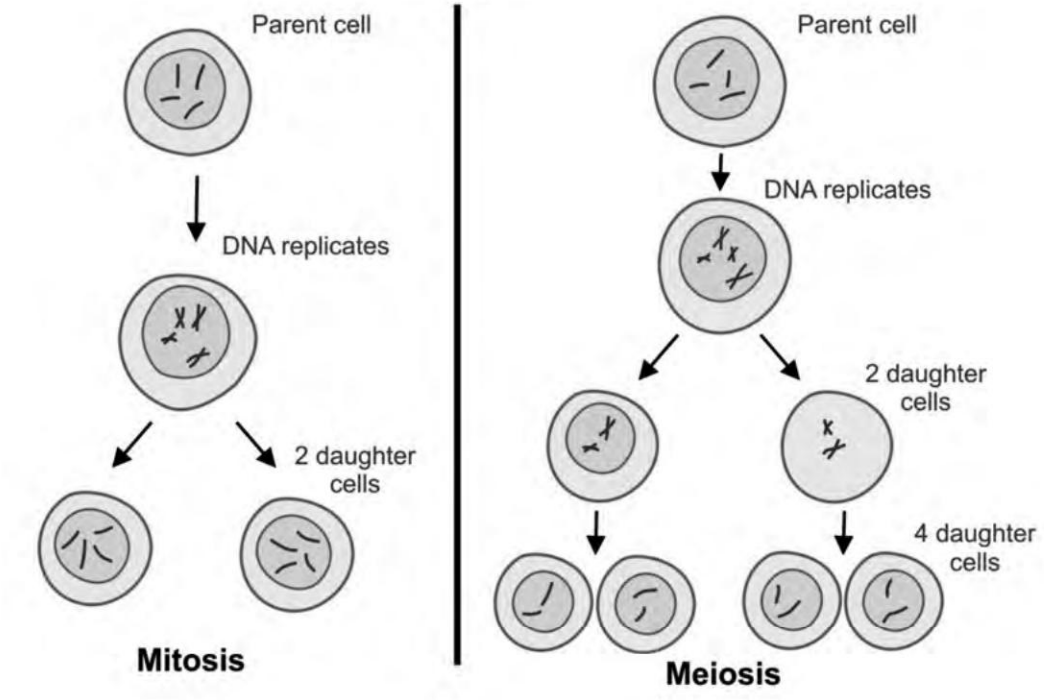


Fig. 2.27 *Comparison of mitosis and meiosis*

REVIEW QUESTIONS

1. Draw and explain the structure of a typical cell.
2. Describe the layers of the cell membrane (structure) with a diagram and state its functions. What is its functional significance?
3. Describe transport across a cell membrane in detail. Differentiate between active and passive transport.
4. Define cell. Define cytoplasm. Enumerate various cell organelles. Describe any two of them in detail.
5. Explain the functions of principle cell organelles.
6. Describe in detail the process of cell cycle. What is its significance?
7. Describe changes during different phases of the cell cycle. Draw suitable diagrams.
8. Describe the structure and functions of nucleus.
9. Write short notes on:
   a. Mitochondria
   b. Endoplasmic reticulum
   c. Carrier proteins
   d. Ion channels
   e. Genetic material
   f. Active transport across cell membrane
   g. Passive transport across cell membrane
   h. Phagocytosis
   i. Sodium-channel blocker
   j. Potassium-channel blocker
   k. Calcium-channel blocker
   l. Mitosis
   m. Meiosis

Chapter

3 Tissue

- **EPITHELIAL TISSUE**
  - Simple
    - Squamous
    - Cuboidal
    - Columnar
    - Ciliated
  - Stratified
    - Stratified squamous
      - Nonkeratinized
      - Keratinized
    - Transitional
    - Pseudo stratified
  - Functions
- **CONNECTIVE TISSUE**
  - Types of connective tissue
    - Dense
    - Loose (areolar)
    - Elastic
    - Reticular
    - Adipose
    - Specialized
      - Blood
      - Bone
      - Cartilage
        - Hyaline cartilage
        - Fibrocartilage
        - Elastic cartilage
  - Cells of connective tissue
    - Fibroblasts
    - Macrophages
    - Mast cells
    - Fat cells
      - Adipose tissue
        - White adipose tissue
        - Brown adipose tissue
    - Leucocytes
      - Lymphoid tissue
  - Functions of connective tissue
  - Nervous and muscle tissue

Introduction

A Tissue is a group of cells that have similar structure and functions together as a unit. The intercellular matrix fills the spaces between the cells. This may be abundant in some tissues and minimal in others. The intercellular matrix may contain special substances such as salts and fibers.

There are four main types of tissues in the body. They are

1 Epithelial
2 Connective
3 Muscle
4 Nervous

3.1 EPITHELIAL TISSUE

Epithelial tissue covers the whole surface of the body and lines the cavities and tubes. It is also found in the glands and is made up of cells, closely packed and arranged in one or more layers.

Epithelial tissue that lies on surfaces of the interior of the body is known as **endothelium**. The cells are closely packed together, with only a small amount of intercellular substance called the **matrix**. Epithelial tissue is separated from the underlying tissue by a thin sheet of connective tissue called the **basement membrane**. The basement membrane provides structural support for the epithelium which also binds it to neighboring structures.

Epithelial tissue can be divided into two groups depending on the number of layers of which it is made of:

- Simple epithelium
- Stratified epithelium

3.1.1 Simple Epithelium

Epithelial tissue which is only one-cell thick is known as simple epithelium. It can be subdivided according to the shape and function of its cells.

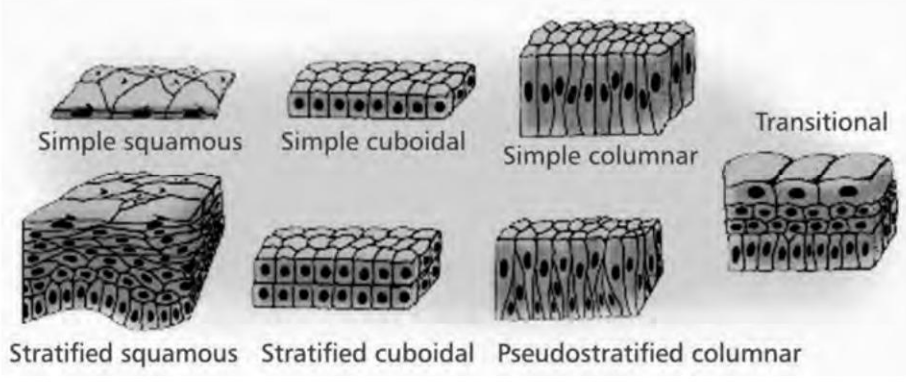


Fig. 3.1 *Types of epithelium*

1. Squamous Epithelium

Squamous cells look like thin, flat plates. The shape of the nucleus usually corresponds to the cell form and helps identify the type of epithelium. Squamous cells have horizontally flattened elliptical nuclei because of the thin, flattened form of the cell. The cells are closely packed together forming a thin and smooth membrane. They form the lining of cavities such as the mouth, blood vessels, lymph vessels, heart and alveoli of the lungs. Here, it is known as the endothelium. It also forms the outer layer of the skin and is called epithelium.

2. Cuboidal Epithelium

Cuboidal cells are cube-shaped cells. Each cell has a spherical nucleus in the center. It is found in glands, in the ducts of glands and in the lining of the kidney tubules. They are also seen in the germinal epithelium which produces the egg cells in the female ovary and the sperm cells in the male testes. They are involved in secretion, absorption and excretion.

3. Columnar Epithelium

Columnar epithelial cells are elongated, tall and column-shaped. The nuclei are elongated and are usually located near the base of the cells. It forms the lining of the organs of the alimentary tract. **Goblet cells** are unicellular glands found between the columnar epithelial cells of the duodenum. They secrete a thick, sticky substance called **mucus** which keeps the surface smooth.

Columnar epithelium with goblet cells is called **glandular epithelium**. These cells become specialized as gland cells. They can synthesize and secrete certain substances such as enzymes, hormones, milk, mucus, sweat, wax and saliva.

Some columnar cells are specialized for sensory reception such as those in the nose, ears and the taste buds of the tongue.

4. Ciliated Epithelium

These are simple columnar epithelial cells, but they have many fine hairlike processes called **cilia** on their free surfaces. The cilia consist of microtubules inside the plasma membrane which extends from the free border.

They are capable of rapid, rhythmic, wavelike movements called **beatings**. This movement of the cilia causes the contents to move in one direction. Ciliated epithelium is usually found in the air passages where they propel mucus towards the throat. It is also found in the uterus and Fallopian tubes of females. The movement of the cilia propels the ovum to the uterus.

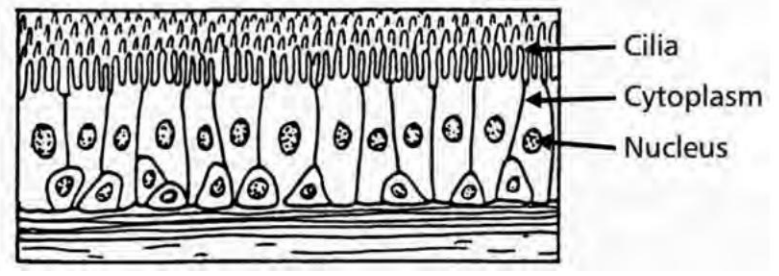


Fig. 3.2 *Ciliated epithelium*

3.1.2 Stratified Epithelium

Where body linings have to withstand wear and tear, the epithelia are composed of several layers of cells. This layer is called compound or stratified epithelium. The top cells are flat and scaly. Superficial layers grow up from below. The basement membrane is usually absent.

It is of two types—Stratified squamous epithelium, and transitional epithelium

1. Stratified Squamous Epithelium

Here there is a combination of newly formed cells and mature cells and they are of different shapes. In the deeper layers, the cells are columnar and as they come up towards the surface, they become flattened.

(a) Nonkeratinized Stratified Epithelium The lining of the mouth cavity, pharynx, esophagus and vagina have this type of epithelium where the surfaces are wet and are subjected to wear and tear.

(b) Keratinized Stratified Epithelium Dry surfaces undergoing wear and tear have this type of epithelium. There are dead epithelial cells to which the protein keratin is added. It acts as a protective layer to the underlying live cells because of its toughness. This layer gets rubbed due to repeated friction and is replaced from below.

2. Transitional Epithelium

This layer is found mainly in the urinary bladder and consists of many layers of pear-shaped cells. The main function here is to allow stretching of the bladder as it fills.

3. Pseudo Stratified Epithelium

A pseudo stratified epithelium is a type of epithelium that, though comprising only a single layer of cells, has its cell nuclei positioned in a manner suggestive of stratified epithelia. As it rarely occurs as squamous or cuboidal epithelia, it is usually considered synonymous with the term pseudo-stratified columnar epithelium.

The term *pseudo-stratified* is derived from the appearance of this epithelium in section which conveys the erroneous (*pseudo* means false) impression that there is more than one layer of cells, while, in fact, this is a true simple epithelium since all the cells rest on the basement membrane. The nuclei of these cells, however, are disposed at different levels, thus creating the illusion of cellular stratification.

3.1.3 Functions of Epithelial Tissue

1. **Protection**—It protects underlying tissue from mechanical injury, injury due to harmful chemicals, from invading bacteria and from excessive loss of water.
2. **Secretory function**—In glands, epithelial tissue is specialized to secrete specific chemical substances such as enzymes, hormones and lubricating fluids.
3. **Absorption**—Certain epithelial cells lining the small intestine absorb nutrients from the digested food.
4. **Excretory function**—Epithelial cells in the kidney excrete waste products from the body and re-absorb needed materials from the urine. Sweat is also excreted from the body by epithelial cells in the sweat glands.
5. **Cleaning**—Ciliated epithelium helps remove sputum, dust particles and foreign substances from the respiratory passages.

6. **Reduce friction**—The cells of the circulatory system form a smooth lining and thus reduce friction between the blood and vessel wall.
7. **Diffusion**—Diffusion of gases and nutrients is possible in simple epithelium as it forms a thin lining. The best example is diffusion of gases in the walls of the capillaries in the lungs.

3.2 CONNECTIVE TISSUE

Connective tissue forms a framework to support organs and the body and is the most abundant tissue. It binds the structures together. There is an abundance of intercellular matrix with relatively few cells. The extracellular substance consists of fibers which are embedded in the ground substance containing tissue fluid. Fibers in connective tissue can be divided into three types: collagen fibers, reticular fibers and elastic fibers. Connective tissue cells are able to reproduce but not as rapidly as epithelial cells. Most connective tissues have a good blood supply.

3.2.1 Types of Connective Tissue

1. Dense connective tissue
2. Loose (areolar) connective tissue
3. Elastic connective tissue
4. Reticular connective tissue
5. Adipose tissue
6. Specialized connective tissue
   - Blood
   - Bone
   - Cartilage

1. Dense Connective Tissue

Dense connective tissue, also called **dense fibrous tissue**, has few cells and abundant fibers, organized into bundles—collagen fibers are its main constituent. In between the fibers are rows of fibroblasts and fiber-forming cells that manufacture the fibers. Dense connective tissue forms strong, ropelike structures such as tendons and ligaments. Tendons attach skeletal muscles to bones; and ligaments connect bones to bones at joints. Ligaments are stretchable because they contain more elastic fibers than tendons. Dense connective tissue also makes up the lower layers of the skin where it is arranged in sheets. It forms an outer protective covering for bone (periosteum) and of some organs like the kidney and brain.

2. Loose or Areolar Connective Tissue

It is the most generalized connective tissue and has a large number of cells. The matrix is not well organized. The cells are mainly fibroblasts with some mast cells, fat cells and macrophages. It is seen below the epithelial tissue and around blood vessels. It is mainly seen in those parts where elasticity and tensile strength is needed. It supports other tissues, e.g., between muscles, in the alimentary canal and in the glands supporting secretory cells.

3. Elastic Connective Tissue

Elastic tissue is a form of connective tissue in which the elastic fibers predominate. Cells are few. Elastic fibers are secreted by the fibroblasts. It is found in the walls of the arteries and in the walls of the bronchial tree. It connects the cartilages of the larynx. Thus, it is found in organs where alteration of shape is required.

4. Reticular Connective Tissue

It is made up of a network of reticular fibers that form a soft skeleton to support the lymphoid organs (lymph nodes, bone marrow and spleen).

5. Adipose Connective Tissue

It contains adipocytes, used for cushioning, thermal insulation, lubrication (primarily in the pericardium) and energy storage (discussed below).

6. Specialized Connective Tissue

(a) Blood Its extracellular matrix is blood plasma, which transports dissolved nutrients, hormones, oxygen and carbon dioxide in the form of bicarbonate. The main cellular component is red blood cells.

Details of this are discussed elsewhere.

The following two can be classified as 'supportive connective tissue'.

(b) Bone Osseous tissue makes up virtually the entire skeleton in adult vertebrates.

Details of this are discussed elsewhere.

(c) Cartilage Cartilage is a type of dense connective tissue. It is composed of specialized cells called **chondrocytes** that produce a large amount of extracellular matrix, composed of collagen fibers and elastic fibers. It is found primarily in joints where it provides cushioning.

Cartilage is classified into three types, viz., elastic cartilage, hyaline cartilage and fibro cartilage, which differ in the relative amounts of these three main components.

Cartilage is found in the articular surface of the bones, the rib cage, the ear, the nose, the bronchial tubes and the intervertebral discs. Its mechanical properties are intermediate between bone and dense connective tissue like tendon.

Hyaline Cartilage Hyaline cartilage consists of a smooth tissue but of considerable elasticity and is pearly bluish in color. It contains no nerves or blood vessels.

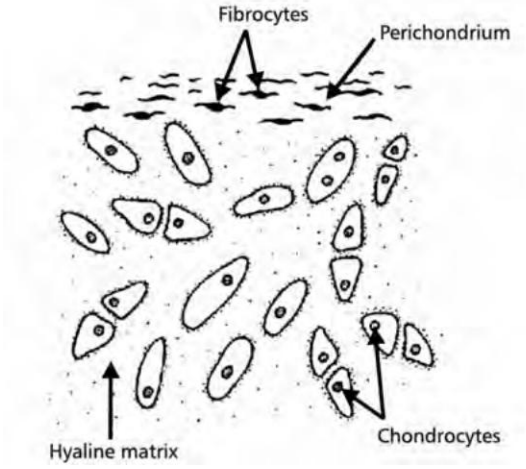


Fig. 3.3 *Hyaline cartilage*

It consists of rounded or bluntly angular cells, lying in groups of two or more in a granular or homogeneous matrix. They consist of clear translucent protoplasm in which fine interlacing filaments and minute granules are sometimes present. The cells have two or more nuclei.

The cells are contained in cavities in the matrix, called cartilage lacunae and around these, the matrix is arranged in concentric lines.

Hyaline cartilage also contains chondrocytes which are cartilage cells that produce the matrix which is solid and smooth.

Hyaline cartilage is seen on the ventral ends of ribs forming the costal cartilages and attaches the ribs to the sternum. It is also present in the larynx, trachea, and bronchi; and on the articular surface of bones.

Fibrocartilage Fibrocartilage is a tough, slightly flexible cartilage with a matrix consisting of dense bundles of fibers. Intervertebral discs and menisci are made of fibrocartilage, which has great tensile strength and is able to absorb considerable loads. (See Fig. 3.4)

It is seen between the articular surfaces of bones of the knee joint, called semilunar cartilage, and also in symphyseal joints. It is seen as ligaments joining bones. It is also seen on the rim of bony sockets of the shoulder and hip joints. The amount of fibrocartilage increases with age as hyaline cartilage transforms into fibrocartilage.

Elastic Cartilage Elastic cartilage is a yellowish flexible cartilage in which the matrix is infiltrated by a network of elastic fibers; it is found primarily in the external ear, Eustachian tube, and some cartilages of the larynx and epiglottis. It is also seen as a part of the tunica media of blood-vessel walls.

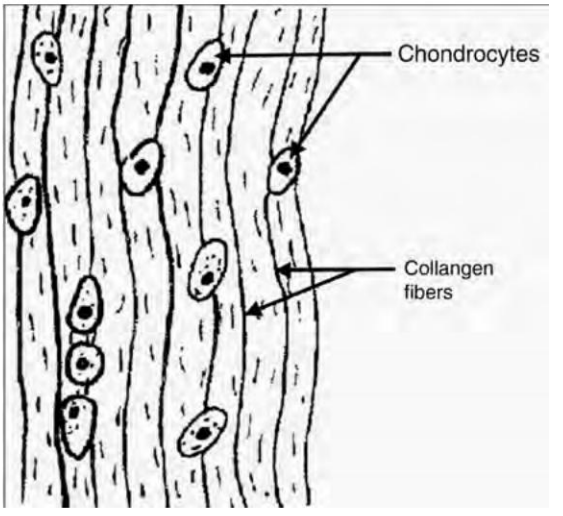


Fig. 3.4 *Fibrocartilage*

3.2.2 Cells of Connective Tissue

Connective tissue found in all the organs is a supporting specialized tissue. The different cells seen in this tissue are

1. Fibroblasts
2. Macrophages
3. Mast cells
4. Fat cells
5. Leucocytes

1. Fibroblasts

Fibroblasts are the most common cells in ordinary connective tissue. They are large, flat cells and have irregular processes. All fibroblasts appear similar to one another and are responsible for secreting collagen and other elements of the extracellular matrix of the connective tissue.

They are essential for normal development and repair. Recent research studies have shown that fibroblasts from different regions show extensively differentiated patterns of gene expression.

They have the ability to become active and to multiply when necessary. They become particularly active in wound healing and form granulation tissue after tissue destruction. Scars are formed by fibroblast activity. The substance of the scar is collagen, deposited by fibroblasts to replace damaged tissue. Active fibroblasts are larger than resting ones.

2. Macrophages

Macrophages engulf, digest and remove the by-products of bacterial infection. Their shape is irregular and they have granules in the cytoplasm. They are an important part of the body's defense mechanism. They are larger than fibroblasts and contain lysosomes which are used for breaking the ingested material.

Macrophages show ameboid movement over short distances. When damage or infection requires reinforcements, monocytes can increase the macrophage population many fold. Macrophages can gather and fuse into giant cells at sites of damage or foreign material.

3. Mast Cells

Mast cells are secretory cells. They are found in loose connective tissue and under the capsule of some organs. They are also seen in good number around blood vessels.

They release chemical substances even on the slightest provocation. These chemical substances diffuse through the surrounding ground substance and trigger inflammation. When cells are damaged, granules containing heparin, histamine and other substances are produced. They are involved in inflammatory reactions. Histamine stimulates secretion of gastric juice and can lead to development of hypersensitivity reactions. Various types of allergies are caused by sensitivity of the mast cells. Heparin prevents blood coagulation.

4. Fat Cells

Adipocytes are large connective tissue cells and are also known as fat cells. They contain a substantial amount of lipid stored in the form of conspicuous round droplets. They occur singly or in groups. Adipocytes function primarily as warehouses for reserve energy. They help in maintaining body temperature. At a few sites, they offer some cushioning effect, e.g., around kidneys and behind the eyeballs. When large masses of these cells are seen, the cluster is called adipose tissue.

Adipose Tissue Adipose tissue, or fat, is an anatomical term for loose connective tissue composed of adipocytes. It consists of fat cells containing large fat globules. The matrix consists of areolar tissue.

Two types of adipose tissue exist: white adipose tissue and brown adipose tissue.

- **White adipose tissue** provides insulation and by storing triglyceride, serves as an energy depot. Its main role is to store energy as fat. It is found under the skin which acts as a thermal regulator. It cushions the eyes and the kidneys. Depending on intake and expenditure of energy, the amount of adipose tissue seen in a person varies.
- **Brown adipose tissue,** or brown fat, is one of the two types of adipose tissue that is present in many newborn babies. Its primary function is to generate heat. Brown adipocytes contain numerous smaller droplets and a much higher number of mitochondria. Brown fat also contains more capillaries than white fat, since it has a greater need for oxygen than most of the other tissues. In adults, it is present in only a small amount.

5. Leucocytes

In healthy connective tissue, leucocytes are seen in small number. During infection, they migrate in large numbers. They play an important role in tissue defense. Lymphocytes, a type of leucocytes, are small cells with round nuclei and a small amount of cytoplasm. They secrete specific antibodies in response to foreign substances and serve as weapons against invading microorganisms.

Lymphoid Tissue Lymphoid tissue is a part of the body's immune system that helps protect the body from bacteria and other foreign substances. It is rich in lymphocytes and accessory cells such as macrophages and reticular cells. The lymphoid tissue includes the lymph nodes, spleen, tonsils and adenoids, appendix, solitary nodes in small intestine and the thymus.

3.2.3 Functions of Connective Tissue

1. It protects against disease. It functions as a physical barrier to the entry of microorganisms into the body.
2. It gives structural and binding support. It connects and binds cells, giving the body structural support and helping tissues to resist mechanical stress, e.g., bone, cartilage, tendon.
3. It helps in transporting substances.
4. It is the place for storage of fat.
5. It helps repair tissue damage.
6. Many connective tissue cells play a role in the defense of the body by mediating inflammation, immunity, and wound repair (macrophages, lymphocytes, fibroblasts, etc.).

3.2.4 Nervous and Muscle Tissues

Nervous and muscle tissues are described in appropriate chapters.

REVIEW QUESTIONS

1. Define tissue. Classify tissues. Write a note on nervous tissue with a labeled diagram.
2. Which are various types of tissue? Describe them.
3. Compare and contrast various muscular tissue. Describe their functions.
4. Classify epithelial tissue. Describe its structure and function.
5. Write short notes on:
    a. Transitional epithelium
    b. Epithelial tissue
    c. Connective tissue
    d. Nervous tissue
    e. Muscular tissue
    f. Adipose tissue
    g. Hyaline cartilage
    h. Stratified columnar epithelium

Chapter

4 Body Fluids and Lymphatic System

- **BODY FLUIDS**
  - Types
    - Intracellular fluid
    - Extracellular fluid
  - Significance
- **LYMPHATIC SYSTEM**
  - Structure
  - Functions
  - Lymph
    - Formation
    - Functions
  - Lymph nodes
  - Lymph glands
    - Spleen
      - Structure
      - Functions
    - Thymus
  - Disorders
    - Lymphadenitis
    - Lymphangitis
    - Hodgkin's disease
    - Splenomegaly
    - Thymus enlargement
    - Edema
    - Pulmonary edema

Introduction

The human body is basically a collection of cells grouped together into organ systems and bathed in fluids. Body fluids mainly contain water, which is principally found in blood, plasma, intracellular and extracellular fluids. Substances are dissolved in it. The body's water content stays constant from day to day. As the body is continually exchanging fluid with the external environment and the different compartments of the body, this constancy is very well maintained.

4.1 BODY FLUIDS

Body fluids contain water and solids. Solids are organic and inorganic substances.

- **Organic substances** are glucose, amino acids, fatty acids, enzymes and hormones.
- **Inorganic substances** are cations like sodium, potassium, calcium and magnesium and anions like chloride, bicarbonate, sulphate and phosphate.

Water is obtained by two major sources—by ingestion of water and food (2000 mL/day) and from oxidation (metabolism) of food (400 mL/day).

Water is lost by a number of ways.

- Water is lost in urine (1500 mL/day). This is the most important way of maintaining balance between water and electrolyte intake and output.
- Water is lost through the skin by evaporation (300 mL/day).
- Water, also, is evaporated through the respiratory tract continually (400 mL/day). This is called insensible water loss, as we are unaware of the process.
- Water is lost by sweat (100 mL/day).
- A small amount of water is lost in feces (100 mL/day).

4.1.1 Types of Body Fluids

There are two main body compartments.

The fluid contained within the cells—intracellular fluid (ICF).

The fluid outside the cells—extracellular fluid (ECF), which is divided into that found within the blood and that found outside the blood.

1. Intracellular Fluid

Intracellular fluid forms nearly 55% of the total body fluid, i.e., nearly 28 liters. This is inside about 75 trillion cells. Under ordinary circumstances, it remains in osmotic equilibrium with the extracellular fluid. The pH of intracellular fluid is 7.0.

This fluid contains a mixture of different constituents in each cell but the concentrations are similar in all the cells. Hence, the intracellular fluid of all different cells together is considered to be one large fluid compartment.

The maintenance of composition of the ICF is by a self-controlled mechanism, i.e., by the cell itself. Selective uptake and output is carried out by the cell membrane. The best example is sodium. Sodium is present in extremely large quantity in the ECF. Hence, even though sodium diffuses into the cell due to the concentration gradient, there is a sodium pump which pushes it back again. This property is essential for carrying out the function of excitation of nerves and muscles. Many substances are present in higher quantity inside the cell, e.g., proteins and ATP.

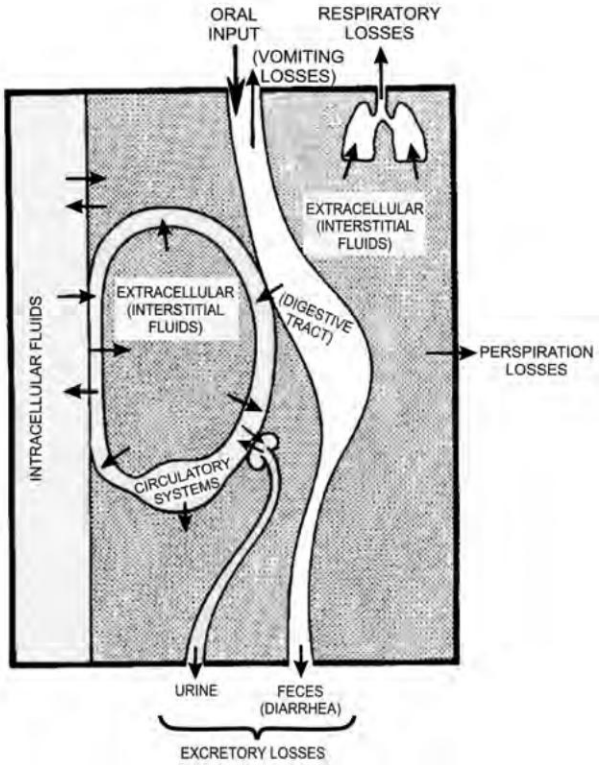


Fig. 4.1 *Absorption of water and its loss through various means*

2. Extracellular Fluid

All the fluids outside the cells are collectively called the extracellular fluid. These form 45% of the total body water, i.e., nearly 14 liters. The pH of extracellular fluid is 7.4.

The extracellular fluid consists of interstitial fluid, plasma, lymph, fluid in the bones and joints, cerebrospinal fluid, intraocular fluid, digestive juices, serous fluid like pleural, pericardial and peritoneal and fluid in the urinary tract.

The two largest compartments of the extracellular fluid are the interstitial fluid, which is about 10.5 liters and plasma,

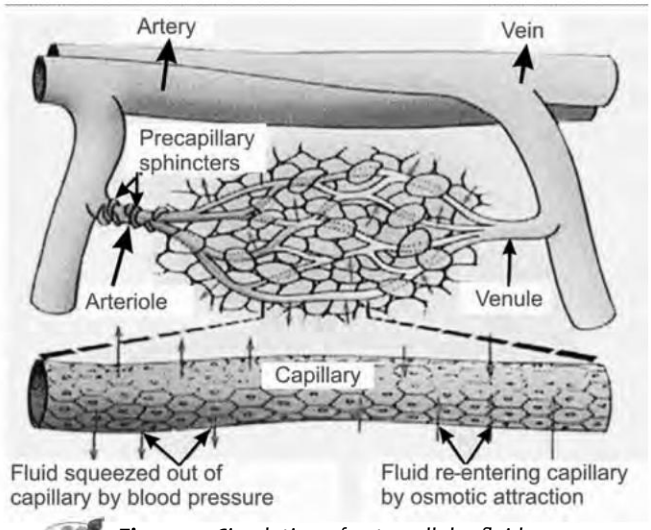


Fig. 4.2 *Circulation of extracellular fluid (Refer colour figure)*

which is about 3 liters. The total volume of other sub-units of extracellular fluid is about 0.5 liters.

Intercellular fluid or interstitial fluid, bathes all the cells of the body except the epidermis of the skin. Plasma is the noncellular part of blood and communicates continuously with the interstitial fluid through the pores of the capillary membranes, which are highly permeable to almost all solutes except proteins. Hence, the extracellular fluids are constantly mixing, so that plasma and interstitial fluids have about the same composition except for proteins. The body cells in contact with the ECF are, hence, dependent on the composition of the interstitial fluid for their normal functioning. Any change can result in damage to the cells and by the process of homeostasis, it reverts to normalcy.

4.1.2 Significance of Body Fluids

Body fluids are mainly responsible for providing moisture and nourishment to the tissues and for maintaining their texture and form. They also moisten, nourish and protect different orifices in the body. For example, body fluids allow the eyes to blink smoothly. Internal body fluids also penetrate different organs, tissues and even bone marrow to provide moisture and nourishment.

Growth and functions of cells depend upon availability of certain materials like glucose, amino acids, lipids, vitamins, ions, oxygen, etc., in proper quantities in the internal environment.

Water plays an important role in homeostasis and in the maintenance of body temperature. Body water forms the transport medium by which nutrients and other essential substances enter the cells and unwanted substances come out of the cells. Enzymes, hormones, vitamins, electrolytes and other substances are carried from one part to another part of the body by body fluids.

4.2 LYMPHATIC SYSTEM

The lymphatic system is an important part of the immune system which protects the body against antigens that invade the body. Lymphatic tissue has a framework of reticular fibers produced by reticular cells which support lymphocytes, macrophages and related cells.

Lymphoid tissue may be found as scattered foci of cells, as dense nodules within the connective tissue—**Peyer's patches**—or as clusters of lymphoid cells such as encapsulated lymph nodes or as lymphoid follicles, e.g., the tonsils. The system also includes lymph vessels and the structures associated with the circulation and production of lymphocytes which are the spleen, thymus and bone marrow.

It carries a clear fluid called **lymph**. This fluid distributes cells and other factors throughout the body. It interacts with blood to drain fluid from cells and tissues.

4.2.1 Structure of the Lymphatic System

The lymphatic system starts as blind lymphatic capillaries in the intercellular spaces in nearly all the organs. Lymphatic vessels join to form lymph vessels. **Anastomoses** are formed between the lymph vessels. These vessels drain into the nearest lymph node and enter lymphatic sinuses in the node. From the lymph nodes efferent vessels emerge and branch to form larger vessels. These vessels finally drain into the right lymphatic duct, thoracic duct or left lymphatic duct. They then empty back into the circulation. The right lymphatic duct opens into the right subclavian vein. The left lymphatic duct opens into the left subclavian vein.

Lymph capillaries are thin-walled vessels closed at one end located in the interstitial spaces throughout the body except the central nervous system, bone and cartilage and in the eye and inner ear. They have a single layer of endothelial cells, the ends of which overlap. When interstitial fluid pressure is more, the cells separate slightly, and interstitial fluid enters the lymphatic capillary. When pressure in the lymphatic capillary is more, the cells come more closely, and lymph is prevented from going back into the interstitial fluid. Thus, the main function is to drain excess tissue fluids from around the cells and return it to the venous circulation, which is now known as lymph.

Lymph capillaries drain into larger lymphatics called **collecting lymphatics**. They drain into larger vessels called **afferent lymph vessels**. They have an outer fibrous covering, middle smooth muscle layer and an inner layer of endothelium. These vessels have valves which ensure that lymph flows in one direction only. They enter a lymph node and **efferent lymph vessels** leave, which form larger ducts, and finally form the **thoracic duct** and **right lymphatic duct** that empty into **the subclavian vein**.

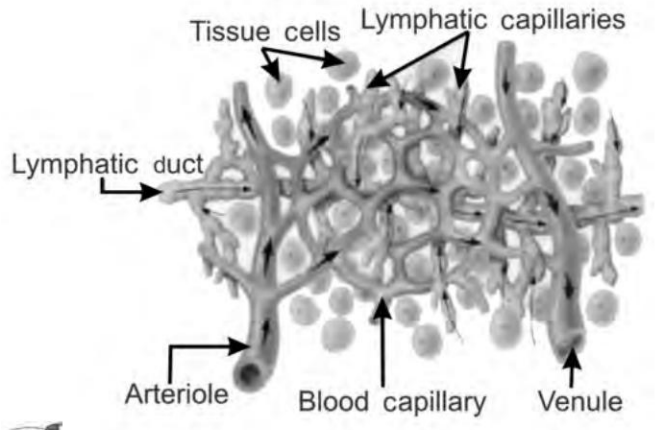


Fig. 4.3 *Lymphatic capillaries (Refer colour figure)*

The segment between two valves is called a **lymphangion** which is the functional unit of a lymph vessel.

The **thoracic duct** is the largest lymphatic vessel in the body. It originates as a dilated lymph vessel, the **cisterna-chyli**, which lies in front of the bodies of the first two lumbar vertebrae. It enters the chest through the aortic hiatus, crosses at the level of the fourth or fifth thoracic vertebra from the right side of the chest to the left and empties into the left subclavian vein. It drains from the legs, pelvis, and abdomen, left half of the thorax, left arm, head and neck.

The **right lymphatic duct** is 1.25-cm long. It lies along the medial border of the scalenus anterior muscle at the root of the neck and ends in the right subclavian vein. It drains from the right arm, right half of the thorax, right side of the head and neck and in some lower lobe of the left lung.

4.2.2 Functions of the Lymphatic System

1. The lymphatic system is mainly responsible for the collection and transportation of fluids from the interstitial spaces in all the tissues of the body and into the blood and thus helps maintain fluid balance.
2. It absorbs and transports fatty acids and fats from the villi in the small intestine as chyle to the circulatory system via lacteals and lymph vessels.
3. It transports antigen cells to the lymph nodes where an immune response is stimulated and defends the body against disease. They filter out microorganisms and foreign substances such as toxins.
4. It transports enzymes and hormones from the site of manufacture to the blood stream.
5. It plays an important role in returning plasma proteins to the circulation.
6. New lymphocytes are manufactured in the lymph nodes.

4.2.3 Lymph

Lymph is the interstitial fluid found between the cells. It enters the lymph vessels by filtration. Lymph has a composition comparable to that of blood plasma, with the exception of plasma proteins. Its composition is the same as the interstitial fluid. The plasma proteins which come out of the capillaries are transported back into the blood through lymph.

Lymph contains white blood cells. The lymph that leaves a lymph node is richer in lymphocytes. Lymph transported from the digestive system is rich in triglycerides (fat), and hence looks white and is called **chyle**.

Lymph picks up bacteria and cell debris from damaged tissues and brings them to the lymph nodes to be destroyed.

Lymph also contains a concentration of infectious and other foreign substances (**antigens**).

Formation of Lymph

Blood supplies nutrients to the cells and collects waste products through the interstitial fluid. The interstitial fluid forms at the arterial end of capillaries and returns (most of it) at the venous end, but, a small amount (1%) enters the lymph capillaries as lymph. Hence, it has the same composition as the interstitial fluid. As it passes through the lymph nodes, it accumulates lymphocytes and proteins from blood.

Functions

1. The lymph glands act as filters and remove bacteria and foreign particles from the tissues.
2. They supply mature lymphocytes to the blood.
3. They return protein and fluid from the interstitial fluid to the circulation and thus maintain a low interstitial-fluid concentration and osmotic-pressure gradient across the capillary membrane.

4.2.4 Lymph Nodes

A lymph node is a small ball-shaped or bean-shaped organ of the immune system linked by lymphatic vessels and distributed throughout the body. Four to five afferent lymph vessels enter a lymph node while only one efferent vessel leaves it. Each node is surrounded by a fibrous capsule which extends into the substance of the node to form trabeculae.

The substance of the node is divided into outer cortex and inner medulla. The hilum is situated on the concave surface of the gland where the medulla comes in direct contact with the surface as it is not covered by the cortex.

The **cortex** contains the B cells arranged as follicles, which may develop as a germinal center, and lymphocytes are developed here when faced by an antigen. T cells are present deeper in the cortex, which interact with dendritic cells. Here, the reticular network is dense.

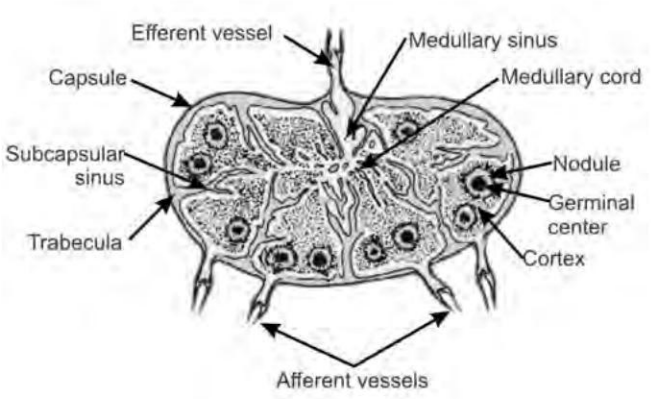


Fig. 4.4 *Lymph-node structure*

In the **medulla** there are cords of lymphatic tissue called **medullary cords**, which include plasma cells and B cells. In between the cords are medullary sinuses which are vessel-like spaces into which the lymph flows from cortical sinuses. Medullary sinuses contain histiocytes and reticular cells.

Hilum is the mouth of the gland where an artery enters and the efferent vessel and vein leaves the node.

Afferent vessels enter the node from all sides and lymph is poured into the node. The lymph that is filtered is rich with lymphocytes. It leaves the node via a single efferent vessel through the hilum.

The main **function** of the lymph node is defense. They filter the lymph and prevent foreign particles and microbes from spreading in the body. They aid immunological responses and manufacture lymphocytes.

4.2.5 Lymph Glands

Name of the glands	*Drainage area*
Cervical	Head and neck
Axillary	Upper limbs
Mediastinal	Thorax
Axillary	Breast
Abdominal esp. mesenteric	Abdomen
Pelvic	Pelvis

1. Spleen

The spleen is a large vascular organ of the lymphatic system, which fights infection and keeps the body fluids in balance. It lies in the hypochondriac region, to the left of the stomach below the diaphragm. It is approximately 6 to 16 centimeters in length and weighs about 200 grams. It is purplish in color.

Structure The spleen consists of a diaphragmatic and visceral surface. It is encased in a thick connective-tissue capsule which dips into the substance of the organ, forming trabeculae. Splenic tissue is of two types, the red pulp and the white pulp, which do not separate into regions but are intermixed and are distributed throughout the spleen. The **white pulp** consists of areas of lymphoid tissue, also called **Malphigian corpuscles**. Lymphocytes and macrophages are present here that surround splenic blood vessels. The **red pulp** is a network of channels (sinuses) filled with blood where most of the filtration occurs.

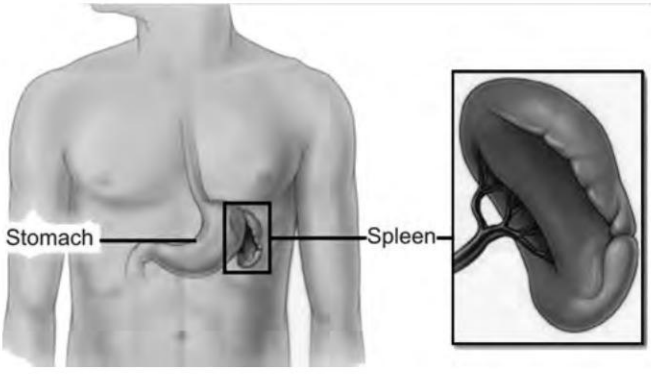


Fig. 4.5 *Spleen*

The visceral surface has a hilum through which pass the arteries, veins and lymphatic vessels.

The white pulp is lymphoid tissue containing lymphocyte-production centres. The red pulp is a network of channels filled with blood where most of the filtration occurs and is the major site of destruction of deteriorating erythrocytes. Both contain cells that remove foreign material and initiate an antibody-producing process.

The spleen has no afferent lymphatics. It has only efferent lymphatic vessels.

Functions

1. The spleen is the primary filtering element for blood. It also serves to store blood. During emergencies, like a cut injury, lost blood is replaced by the spleen.
2. It is a storage site for red blood cells (erythrocytes) and platelets.
3. It is one of the four places where the reticuloendothelial cells are found.
4. The red pulp is the body's major site of the destruction of red blood cells. Degenerated red cells are removed and the degraded products—bilirubin and iron—are passed to the liver. Bilirubin is partly oxidized to biliverdin. The iron molecule is recycled to be used for new hemoglobin production.
5. The white pulp contains plasma cells, lymphocytes and lymphatic nodules, called follicles. It reacts to microorganisms and other antigens that reach the blood-stream.
6. Germinal centers in the white pulp are sites of lympho-cyte production.
7. Phagocytic cells in both red and white pulp serve to remove foreign material from the blood and initiate an

immune reaction that results in the production of antibodies.

8. The spleen is also the site of fetal-blood-cell production.

2. Thymus

The thymus is a pinkish-gray colored, soft specialized organ of the immune system. It enlarges during childhood and atrophies at puberty. It rarely persists up to adulthood. It is situated in the anterior superior mediastinum, behind the sternum, below the thyroid gland and on the trachea. It consists of two lobes enclosed in a fibrous capsule which dips into the substance of the gland. Each lobe is composed of lobules, held together by areolar tissue. The lobules are made up of a number of follicles which are irregularly shaped but fused together. Each follicle has a cortex and a medulla.

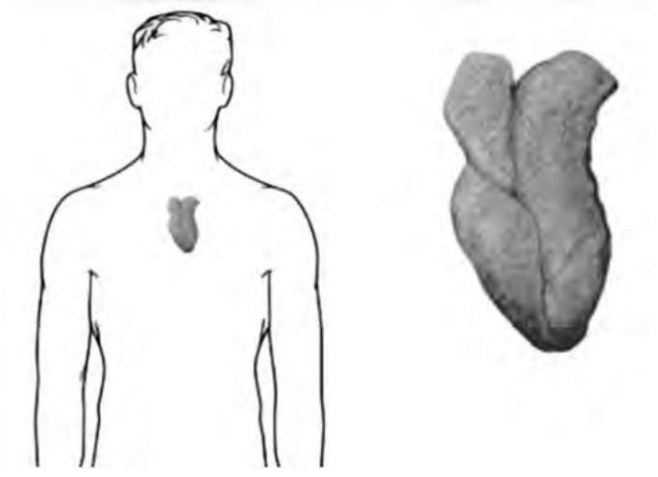


Fig. 4.6 *Thymus gland*

The cortical portion consists of lymphoid cells, supported by a network of epithelial reticular cells, continuous with the network in the medullary portion. The reticulum is coarser in the cortex. These peculiar nestlike bodies called **Hassal's corpuscles** are specific for thymus. They have a central hyaline mass, surrounded by concentrically arranged flat cells.

Thymus atrophies at the time of puberty. Its functions are deposition of mineral salts in the bone, formation of lymphocytes, promoting growth of sex glands and development of puberty and probably secretion of a substance which depresses muscular contraction.

4.2.6 Disorders of the Lymph and Lymphatic System

1. Lymphadenitis

Lymphadenitis is an infection of the lymph nodes and a common complication of certain bacterial infections. The microbes are transported in the lymph from infection elsewhere in the body. The nodes are inflamed, enlarged and sometimes this may lead to abscess formation. Adjacent tissues may get affected and the infection may re-enter the blood.

Pathophysiology It occurs when the glands become overwhelmed by bacteria, virus, fungi or cancer cells. It may occur after cellulites.

2. Lymphangitis

Lymphangitis is an acute inflammation of the smaller lymphatics. It results from an acute streptococcal infection of the skin and less commonly from a staphylococcal infection.

3. Hodgkin's Disease

Hodgkin's disease is a type of lymphoma, where there is painless, progressive enlargement of the lymph nodes throughout the body, beginning in one group and then spreading to other groups. It is a cancer originating from the lymphocytes.

Four stages are described. In Stage I, a single lymph node region is involved. In Stage II, there is involvement of two or more lymph nodes or one lymph node region and a contiguous extra-lymphatic site. In Stage III, lymph nodes on both the sides are involved; and in Stage IV, there is disseminated involvement with involvement of the spleen, liver and other extra-lymphatic organs.

Pathophysiology The disease is malignant and the cause is not known. There is reduced immunity and lymphocyte function is suppressed.

4. Splenomegaly

Splenomegaly is an enlargement of the spleen and is almost always secondary to other disorders. It is usually associated with increased workload. Hence, it suggests that it is a response to hyperfunction. It is one of the four cardinal signs of hypersplenism, the other three being cytopenia, hyperplastic or normal bone marrow and a response to splenectomy.

Pathophysiology Any disease process associated with abnormal red-cell destruction in the spleen is associated with splenomegaly. Splenomegaly may arise as a symptom in a number of conditions like inflammatory diseases, hematological diseases, systemic infections, inherited spleen disorders and neoplastic diseases.

Splenomegaly can also occur due to a condition called congestive splenomegaly, where the spleen gets engorged with blood due to impaired flow through the splenic vein which empties into the portal vein. This is seen in portal hypertension, liver disease, constrictive pericarditis, leukemias and congestive cardiac failure.

5. Thymus Enlargement

Enlargement of the thymus gland occurs in certain auto-immune diseases such as myasthenia gravis, thyrotoxicosis and Addison's disease. The enlarged gland may press or damage the adjacent structures like the trachea or esophagus.

6. Edema

Edema occurs when there is a build-up of fluid, mainly water in the body tissues, which causes swelling to occur in the affected area. It could be localize due to a local abnormality or generalized due to a systemic condition. Any tissue or organ can be affected especially the hands, feet and around the eyes. It can also occur by a variety of factors such as high salt intake in the diet or being immobile for a long time.

Pathophysiology Tissue fluid may accumulate when

- Capillaries become more permeable
- Pressure is high inside the capillaries or low outside
- There is deficiency of plasma proteins
- Lymphatic drainage is blocked

When the balance of forces which moves water to and fro across the capillary walls is disturbed, water accumulates in the tissues.

Due to increase in hydrostatic pressure inside the capillaries than outside, some water from the plasma, with the dissolved particles, moves into the tissues. The effect of osmotic pressure is reduced at the venous end which draws fluid back into the capillaries. This is seen in kidney diseases, heart failure and prolonged pressure over a limb.

When there is deficiency of plasma proteins, less fluid returns to the circulation and fluid accumulates as seen in nephrotic syndrome, liver failure and malnutrition.

Increased capillary permeability, as seen in inflammation, causes plasma proteins to leak out into the tissues and leads to increased tissue osmotic pressure. Fluid is drawn out and there is edema. This is seen in allergic reactions.

Usually lymph drains, filters and then returns the fluid to the circulation. When lymphatic drainage is affected, fluid is retained in the tissues and edema occurs. This is seen in lymph-node destruction in chronic inflammation, malignancy blockage and in surgical removal of nodes.

7. Pulmonary Edema

There is venous congestion of the lungs, or increased capillary permeability, leading to fluid accumulation in the alveoli. The area for gaseous exchange decreases and there is difficulty in breathing, leading to cyanosis and expectoration.

REVIEW QUESTIONS

1. Write a note on body fluids.
2. Write a note on lymph.
3. Describe the composition and functions of lymph.
4. Describe the structure and functions of the lymphatic system.
5. Describe the structure and functions of spleen.
6. What is edema? Describe its pathophysiology. Write a note on pulmonary edema.
7. Write short notes on:
   a. Spleen
   b. Lymph nodes
   c. Lymphadenitis and lymphangitis
   d. Thymus
   e. Hodgkin's disease
   f. Splenomegaly

Chapter

5 Skeletal System

- **BONES**
  - **Types of bones** — Long; Short; Irregular; Flat; Sesamoid
  - **Structure of bones** — Long bones; Short, irregular, flat and sesamoid; Macroscopic — Compact bone; Spongy or trabecular; Microscopic or Bone cells — Osteoblasts (Functions); Osteocytes (Functions); Osteoclasts (Functions)
  - **Bone development** — Ossification — Intramembranous; Endochondral
  - **Functions of bones**
  - **Skull** — Bones of the calvaria — Paired (Parietal, Temporal); Unpaired (Frontal, Occipital, Ethmoid, Sphenoid); Bones of the face — Paired (Maxilla, Nasal bones, Lacrimal bones)

- Zygomatic bones
- Palatine
- Inferior chonchae
- Unpaired
  - Mandible
  - Vomer

- Cranial cavity
  - Divisions
    - Anterior cranial fossae
      - Applied anatomy
    - Middle cranial fossa
      - Applied anatomy
    - Posterior cranial fossa
      - Applied anatomy
- Vertebral column
  - Characteristics of typical vertebra
  - Special features in different vertebrae
    - Cervical
    - Thoracic
    - Lumbar
    - Sacrum and coccyx
  - Functions of vertebral column
- Thoracic cage
  - Sternum
  - Ribs
- Appendicular skeleton
  - Shoulder girdle and upper limb
  - Clavicle
  - Scapula
  - Humerus
  - Radius
  - Ulna
  - Bones of the wrist and hands
    - Carpal, metacarpal and phalanges
- Hip and lower limb
  - Hip bone
  - Femur
  - Tibia
  - Fibula
  - Patella
  - Bones of the foot
    - Tarsal, metatarsal and phalanges
  - Arches of foot

- Disorders of bones
  - Osteoporosis
  - Osteomalacia
  - Osteomyelitis
  - Paget's disease
  - Achondroplasia

• JOINTS

- Classification
  - Fibrous
  - Cartilaginous
  - Synovial
    - Characteristics of Synovial joint
- Types
  - Ball-socket joint
  - Gliding joint
  - Hinge joint
  - Pivot joint
  - Saddle and condyloid joint
- Main synovial joints
  - Joints of upper limb
    - Shoulder joint
    - Elbow joint
    - Radio-ulnar joint
    - Wrist joint
    - Joint of wrist and fingers
  - Joints of lower limb
    - Hip joint
    - Knee joint
    - Ankle joint
    - Joint of the foot and toes
- Movements
  - Gliding joint
  - Angular
  - Circumduction
  - Rotation
- Disorders of joints
  - Arthritis Rheumatoid arthritis
  - Osteoarthritis
  - Ankylosing spondylitis
  - Psoriatic arthritis
  - Rheumatic arthritis
  - Reiter's syndrome
  - Septic arthritis
  - Gout

Introduction

Bones are rigid organs that form a part of the endoskeleton of vertebrates.

They function to support, move and protect the various organs of the body, produce red and white blood cells and store minerals.

Bone tissue is a type of dense connective tissue. Such tissues have special types of cells with a matrix of collagen fibers, which form the tough ground substance. In the matrix, there is deposition of mineral salts like calcium **carbonates** and phosphates. This strengthens the bone.

Because bones come in a variety of shapes and have a complex internal and external structure, they are light in weight, yet strong and hard. One of the types of tissues that makes up bones is the mineralized **osseous tissue**, also called bone tissue that gives bones rigidity and a honeycomb-like, three-dimensional internal structure. Other types of tissues found in bones include marrow, endosteum and periosteum, nerves, blood vessels and cartilage.

Resorption and formation of bone goes on all throughout the life of an individual and thus bones get renewed.

5.1 BONES

5.1.1 Types of Bones

There are five types of bones in the human body:

1. Long bones
2. Short bones
3. Irregular bones
4. Flat bones
5. Sesamoid bones

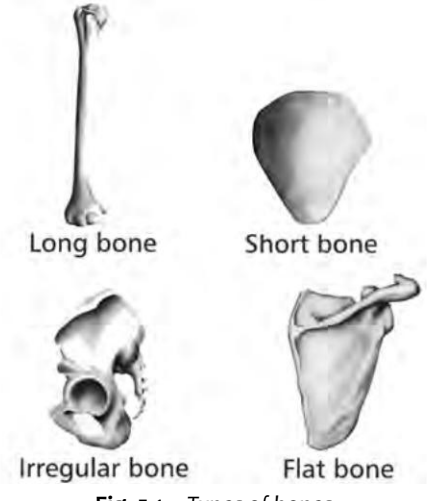


Fig. 5.1 *Types of bones*

1. Long Bones

Long bones are characterized by a shaft, the diaphysis that is much greater in length than width. They comprise, mostly, compact bone and lesser amounts of marrow (located within the medullary cavity) and spongy bone. Most bones of the limbs, including those of the fingers and toes, are long bones. Exceptions are bones of the wrist, ankle and kneecap.

2. Short Bones

Short bones are cube-shaped, and have only a thin layer of compact bone surrounding a spongy interior. The bones of the wrist and ankle are short bones.

3. Irregular Bones

Irregular bones consist of thin layers of compact bone surrounding a spongy interior. Their shapes are irregular and complex. The bones of the spine and hips are examples of irregular bones.

4. Flat Bones

Flat bones are thin and generally curved, with two parallel layers of compact bones sandwiching a layer of spongy bone. Most of the bones of the skull and the sternum are flat bones.

5. Sesamoid Bones

Sesamoid bones are bones embedded in tendons. Since they act to hold the tendon further away from the joint, the angle of the tendon is increased and thus the force of the muscle is increased. Examples of sesamoid bones are the patella and the pisiform bone.

5.1.2 Structure of Bones

1. Structure of a Long Bone

Long bones have the following parts:

1. Diaphysis or shaft
2. Epiphysis or extremities
3. Metaphysis—between diaphysis and epiphysis

Most of the bones have two layers of structures:

1. Outer compact bone
2. Inner spongy bone or trabecular bone

Diaphysis has compact bone with a central medullary canal containing fatty yellow bone marrow and spongy bone which is very thin.

Epiphysis has a large amount of spongy bone with an outer covering of compact bone, which is thin.

Between the diaphysis and epiphysis, there are epiphyseal cartilages which ossify when human growth is complete. This is **metaphysis**.

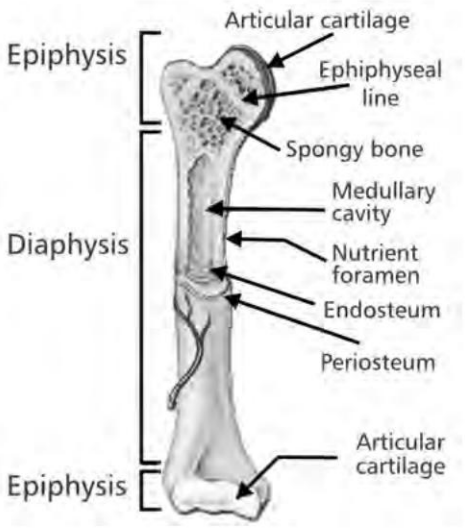


Fig. 5.2 *Long bone*

Long bones are covered by a white fibrous connective layer called the **periosteum**. There is an inner layer, which consists of dense fibrous membrane and is called **endosteum**. The periosteum gives attachment to the tendons of muscles.

The epiphysis is covered by hyaline cartilage which forms the synovial joint with adjoining bones.

2. Structure of Short, Irregular, Flat and Sesamoid Bones

These bones have a thin layer of compact bone with cancellous bone inside, having red bone marrow. They have periosteal covering. This is not seen in the inner layer of cranial bones but has a covering of dura mater.

3. Macroscopic Structure of Bone

Bone is not a uniformly solid material, but rather has some spaces between its hard elements.

(a) Compact Bone The hard outer layer of bones is composed of compact bone tissue, so called because it has minimal gaps and spaces. This tissue gives bones their smooth, white and solid appearance, and accounts for 80% of the total bone mass of an adult skeleton. Compact bone may also be referred to as **dense bone**.

Compact bone has minute cylindrical structures called **Haversian systems** or **osteones**. There are concentric layers of collagen called **Haversian lamellae**. There is a central Haversian canal containing blood vessels, lymph vessels and nerve fibers. There is communication of the Haversian systems with one another by transverse canals called **Volkmann's canals**. In between are tiny spaces called **lacunae** which contain tissue fluid and spider-shaped osteocytes. These osteocytes have long processes called **canaliculi** which join each other and form links.

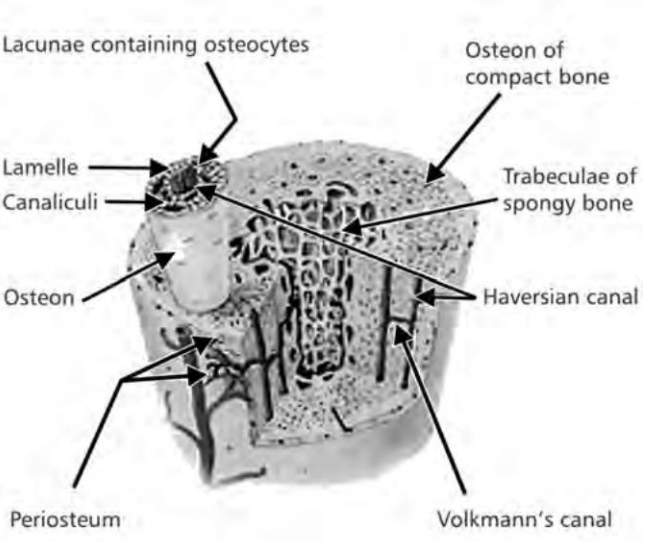


Fig. 5.3 *Compact bone and spongy (cancellous) bone (Refer colour figure)*

Interstitial lamellae are found between the Haversian systems. The tubular arrangement gives more strength to the bone rather than a solid structure.

(b) Spongy or Trabecular Bone Filling the interior of the bone is the trabecular bone tissue, also called cancellous or spongy bone, which is composed of a network of rod and plate-like elements that make the overall organ lighter, allowing room for blood vessels and marrow. Trabecular bone accounts for the remaining 20% of total bone mass, but has nearly ten times the surface area of compact bone.

It consists of bony spicules. There is a framework formed from trabeculae which has lamellae and osteocytes. Canaliculi connect the osteocytes. The space in between contains red bone marrow which nourishes the osteocytes.

4. Microscopic Structure or Bone Cells

There are three types of bone cells:

(a) Osteoblasts
(b) Osteocytes
(c) Osteoclasts

(a) Osteoblasts Osteoblasts are mononucleate bone-forming cells. They are cells which secrete collagen and other constituents of bone tissue. They are concerned with bone formation and are found on the outer surface of bone and marrow cavity. They are also seen at the site of a fracture and adjacent to the epiphyseal cartilages of long bones.

Functions

1. They synthesize bone matrix.
2. Osteoblasts also manufacture hormones, such as **prostaglandins**, to act on the bone itself.

3. They produce alkaline **phosphatase** (an enzyme that has a role in the mineralization of bone) as well as many matrix proteins.
4. Bone-lining cells are essentially inactive osteoblasts. They cover all of the available bone surface and function as a barrier for certain ions.

(b) Osteocytes Osteocytes originate from osteoblasts, which have migrated into the matrix and get trapped and surrounded by bone matrix, which they themselves produce. The spaces which they occupy are known as lacunae. Cytoplasmic processes from osteocytes join to form canaliculi and in turn form tight junctions. They are spread throughout the bone matrix.

Osteocytes have many processes which reach out to meet osteoblasts and other osteocytes probably for the purposes of communication.

Functions

1. They help in the movement of calcium between the bone and blood.
2. They help in the formation of bone and matrix maintenance due to their metabolic activity.
3. They have also been shown to act as mechano-sensory receptors—regulating the bone's response to stress and mechanical load. They are mature bone cells.

(c) Osteoclasts Osteoclasts are the cells responsible for bone resorption. They are large, multinucleated cells found in the lacunae of bone matrix. These lacunae are left behind after the breakdown of the bone surface. They maintain the shape of the bone. Because the osteoclasts are derived from a monocyte stem-cell lineage, they are equipped with phagocytic-like mechanisms similar to circulating macrophages.

Functions Normal bone structure and function is maintained due to a fine balance between osteoblasts and osteoclasts.

5.1.3 Bone Development

Ossification of bone starts even before birth and goes on till the age of 21 years.

Bone development takes place in two stages:

Osteoblasts secrete **osteoid**—collagen fibers—in the matrix. Original cartilage and membrane are replaced by this osteoid which gets calcified and there is bone formation.

Collagen fibers are arranged in two ways.

They are deposited as irregular bundles which then get ossified. This is seen in bones that originate as membrane bones, e.g., skull bones.

In another arrangement, the collagen fibers are deposited as in woven bone in the form of lamellae and get ossified. This is seen in cartilage bones.

Long, short and irregular bones develop from rods of cartilage. Flat bones develop from membrane and sesamoid bones from tendon models.

Ossification of Bone

Ossification is the process of bone formation, in which connective tissues, such as cartilage are turned to bone or bonelike tissue. The ossified tissue is invaginated with blood vessels. These blood vessels bring minerals like calcium and deposit it in the ossifying tissue. Bone formation is a dynamic process, with cells called osteoblasts depositing minerals and osteoclasts removing the bone.

Types of Ossification Bones may be synthesized by intramembranous ossification, endochondral ossification, or a combination of the two.

- **Intramembranous ossification** is the transformation of the mesenchyme, embryonic cells, into bone. During early development, the embryo consists of three primary cell layers—**ectoderm** on the outside, **mesoderm** in the middle and **endoderm** on the inside. Mesenchyme cells constitute a part of the embryo's mesoderm and develop into connective tissue such as bone and blood. The bones of the skull derive directly from mesenchyme cells by intramembranous ossification.

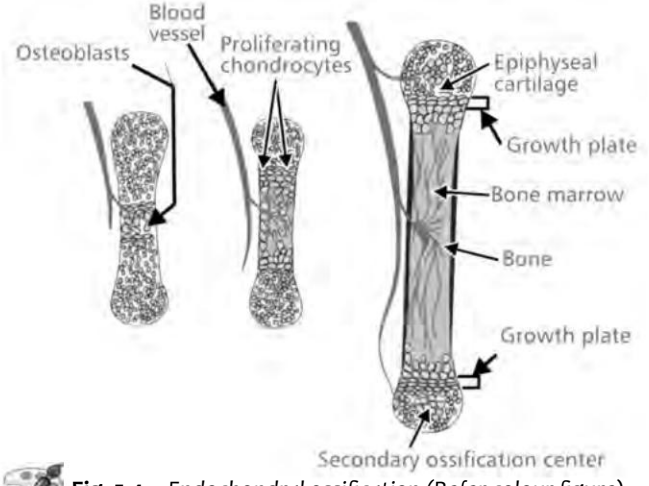


Fig. 5.4 *Endochondral ossification (Refer colour figure)*

- **Endochondral ossification** is the gradual replacement of cartilage by bone during development. This is responsible for formation of most of the skeleton. Osteoblasts arise in regions of cartilage, called **ossification centers**. They develop into osteocytes, which are mature bone cells, embedded in the calcified (hardened) part of the bone known as the matrix.

Most bones arise from a **combination of intramembranous and endochondral ossification**. Mesenchyme cells develop into chondroblasts and increase in number by cell

division. Chondroblasts enlarge and excrete a matrix which hardens due to presence of inorganic minerals. Chambers form within the matrix and osteoblasts and blood-forming cells enter these chambers. The osteoblasts then secrete minerals to form the bone matrix.

Mature hardened bone consists of an organic component and a mineral component. The organic part consists of proteins such as collagen fibers, an extracellular matrix and fibroblasts (which produce the collagen and matrix). The mineral part of bone gives strength and rigidity. During the life of an individual, osteoblasts continually secrete minerals while osteoclasts continually reabsorb the minerals.

5.1.4 Functions of Bones

1. Bones form the skeleton which is the framework of the body.
2. The skeleton supports the softer tissues and provides points of attachment for most skeletal muscles.
3. The skeleton provides mechanical protection for many of the body's internal organs, reducing risk of injury to them. It forms boundaries of cranial, thoracic and pelvic cavities. Thus, it protects the brain, lungs, heart, etc.
4. Bones permit movement of the body as a whole or part of the body, by formation of joints, which are moved by muscles.
5. Bone tissues store several minerals, including calcium and phosphorus. When required, bones release minerals into the blood facilitating and maintaining the balance of minerals in the body.
6. Bones contain red bone marrow in which blood cells develop.
7. Bones act as an important chemical reserve. With advancing age, some bone marrow changes from red bone marrow to yellow bone marrow which consists mainly of adipose cells and a few blood cells.

5.1.5 Skull (Cranium)

The bones of the head and neck include the skull, the hyoid bone and the cervical vertebrae.

The skeletal part of the head is called the skull. The skull rests on the upper end of the vertebral column. It consists of several bones that are joined together to form the cranium. The skull also includes the lower jaw which is also called the mandible, although it is a separate bone.

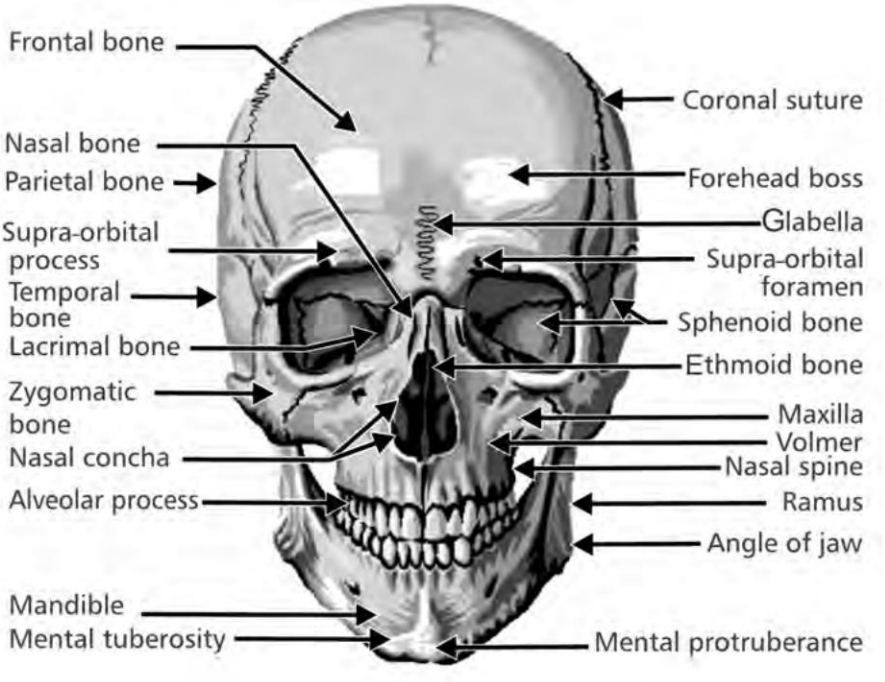


Fig. 5.5 *Frontal view of skull*

The skull is also called the cranium. It is divided into two parts:

1. The calvaria are the upper part of the cranium which encloses the brain.
2. The other part is the facial skeleton, which forms the rest of the skull and also includes the mandible.

The skull consists of 22 bones—8 of the calvaria and 14 facial bones.

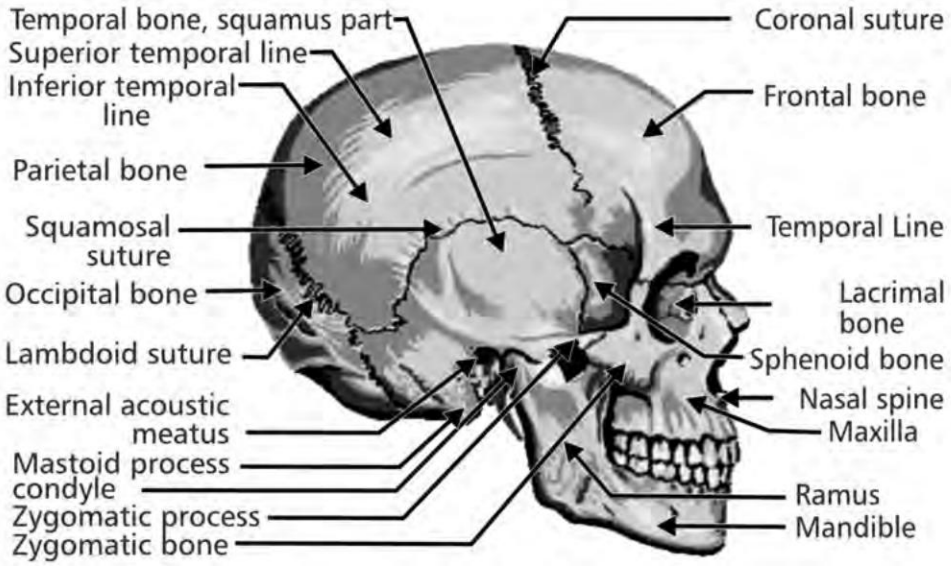


Fig. 5.6 *Lateral view of skull*

1. Bones of the Calvaria

These bones are flat and irregular. There is a base on which the brain rests and there is a vault which covers the brain. With the exception of the temporo-mandibular joint, the joints are immovable and are of fibrous type. These joints are called **sutures**. The bones on the inner side are lined by dura mater. The skull bones have many foramina and fissures through which pass the nerves, blood and lymph vessels. They can be divided into two types:

- **Paired**: Parietal and Temporal
- **Unpaired**: Frontal, Occipital, Ethmoid and Sphenoid

(a) Parietal Bones The parietal bones form the sides and roof of the skull. The inner surface is grooved by the brain and blood vessels and is concave in shape. The parietal eminence is the area of maximum convexity of the parietal bone. The parietal bones form the sagittal suture by articulating with each other. It forms the coronal suture with the frontal bone and with the occipital bone articulates at the lambdoidal suture. With the temporal bones they articulate to form the squamous suture. The parietal foramen, one on each side, pierces the parietal bone near the upper border, 3 to 4 cm in front of the lambda. The **lambda** is the meeting point between the sagittal and lambdoid sutures.

(b) Temporal Bones The temporal bones lie one on each side. They form joints with sphenoid, parietal, occipital and zygomatic bones. These joints are immovable joints.

The temporal bone has a squamous part which is thin and fan-shaped and articulates with the parietal bone. The mastoid part lies just behind the external acoustic meatus. The mastoid process is a large projection from the lower part of this mastoid temporal bone. The mastoid part has many small air sinuses which are lined by squamous epithelium. They communicate with the middle ear.

The zygomatic process of the temporal bone joins the temporal process of the zygomatic bone and forms the **zygomatic arch**.

The temporal bone articulates with the mandible to form the temporo-mandibular joint. This is the only movable joint of the skull. The external auditory meatus opens just behind this articulating surface and passes medially towards the petrous part of the temporal bone.

The petrous portion forms the base of the skull and contains the organs of hearing.

The mastoid foramen lies near the occipitomastoid suture.

(c) Frontal Bone The frontal bone forms the forehead. It forms part of the orbital cavities and the supra-orbital margins. The upper part is smooth and convex while the lower part is irregular and contains the orbit and the anterior bony aperture of the nose. Above the supra-orbital margins, there are two cavities within the bone called **sinuses**. They are filled with air and are called **frontal sinuses**. They are lined with ciliated mucous membrane and open into the nasal cavity.

The frontal bones form joints with other bones of the skull and face. They form joints with the parietal bones, called the **coronal suture**. Frontal bones also form joints with sphenoid, zygomatic, lacrimal, ethmoid and nasal bones. In the midline, the two frontal bones join to form the **frontal suture**.

(d) Occipital Bone The occipital bone forms the back part of the skull and the base of the cranium. It joins with the parietal, sphenoid and temporal bones and forms immovable joints. In the center, on the inferior portion of the cranium,

there is a large opening called the **foramen magnum**, through which the lowest part of the brain stem descends, and is now called the spinal cord with its three coverings.

The inner surface is concave and is occupied by the cerebellum and occipital lobes of the cerebrum.

The occipital bone has a squamous part marked by superior and inferior nuchal lines.

The condylar part of the occipital bone has the following structures:

(i) Occipital condyles are oval in shape and situated on each side of the anterior part of the foramen magnum. They form hinge joints with the first bone of the vertebral column called the **atlas**.
(ii) The hypoglossal canal pierces the bone.
(iii) The condylar canal is present in the floor of the condylar fossa.
(iv) The jugular process of the occipital bone lies lateral to the occipital condyle.

(e) Ethmoid Bone The ethmoid bone is exceedingly light, spongy and cubical in shape. It occupies the anterior part of the base of the skull. It helps to form the orbital cavity.

It consists of four parts—a horizontal or cribriform plate, forming part of the base of the cranium; a perpendicular plate, which forms part of the nasal septum; and two lateral masses or labyrinths. The cribriform plate of the ethmoid bone separates the anterior cranial fossa from the nasal cavity and forms the roof of the nasal cavity. From this bone, on both the sides, there are two projections into the nasal cavity, called **conchae** or **turbinated processes**. It contains many air sinuses lined by ciliated epithelium. These sinuses open into the nasal cavity. Through the openings in the cribriform plate pass the nerve fibers of the olfactory nerve which end in the olfactory bulb. The perpendicular plate of the ethmoid bone forms the upper part of the nasal septum.

(f) Sphenoid Bone The sphenoid bone is situated in the middle portion of the base of the skull in front of the temporals and basilar part of the occipital bone. It somewhat resembles a bat with its wings extended and is divided into a median portion or body, two great and two small wings extending outward from the sides of the body and two pterygoid processes which project from it.

The body is cubical in shape and is hollowed out in its interior to form two large cavities, the sphenoidal air sinuses, which are separated from each other by a septum. These sinuses are lined by ciliated mucous membrane and open into the nasal cavity.

It forms articulations with the temporal, parietal, occipital and frontal bones. In the middle of the bone on the superior surface, there is a saddle-shaped depression which is called the **hypophyseal fossa**. In this fossa lies the pituitary gland.

2. *Bones of the Face*

The face is also known as the countenance. It extends superiorly from the hairline to the chin and inferiorly to the base of the mandible. It lies between the two auricles.

The facial skeleton consists of 13 stationary bones in addition to the frontal bone and a lower jawbone called the mandible. These 14 bones form the basic shape of the face, are responsible for providing attachments to the muscles that make the jaw move and control the muscles of facial expression.

Paired: Maxilla, Nasal, Lacrimal, Zygomatic, Palatine and Inferior nasal concha

Unpaired: Mandible and Vomer

(a) Maxilla The maxillary bones are the largest bones of the face and together form the upper jaw. The maxilla originates as two bones but fusion takes place before birth. The maxilla forms the hard palate, floor of the nose and lateral wall of the nasal cavity, part of the floor of the orbital cavities, upper jaw and the tooth sockets of the upper teeth. Above the roots of the upper teeth and below the floor of the orbits are the maxillary sinuses, the largest of the sinuses. The maxillary sinus opens into the nasal cavity and is lined by ciliated membrane.

The anterior surface of the body of the maxilla presents the nasal notch, anterior nasal spine, the infra-orbital foramen, the incisive fossa and the canine fossa.

Each maxilla consists of a body and three processes—zygomatic, frontal and alveolar. The **frontal process** is directed upwards and articulates with the nasal bone, lacrimal bone and frontal bone. The **zygomatic process** articulates with the zygomatic bone. The **alveolar process** projects downwards and bears sockets for the upper teeth.

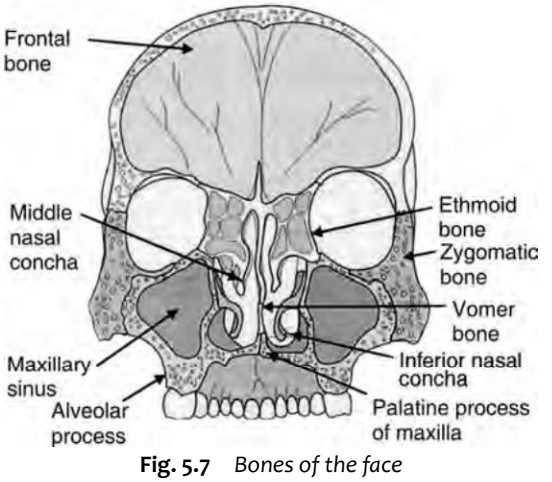


Fig. 5.7 *Bones of the face*

(b) Nasal Bones Nasal bones are two small flat bones. They form the greater part of the lateral and superior surfaces of the bridge of the nose.

(c) Lacrimal Bones Lacrimal bones are two small bones lying posterior and lateral to the nasal bones. They form part of the medial walls of the orbital cavities. There is a foramen for the passage of the naso-lacrimal duct which carries tears from the medial canthus of the eye to the nasal cavity.

(d) Zygomatic Bones The zygomatic bones make up the prominence of the cheeks and extend from the zygomatic process of the temporal bone to the zygomatic process of the maxilla. The zygomatic bones form the 'cheek bones' and help to form the sides and floor of the orbits. The zygomatico-facial foramen is seen on its surface.

(e) Palatine Bones Palatine bones are paired. They are 'L' shaped. They take part in the formation of the following:

1. Posterior 1/3rd of hard palate which is formed by the horizontal components
2. Part of the lateral walls of the nasal cavity is formed by the perpendicular parts which project upwards
3. Part of the orbital cavities at their upper extremities

(f) Inferior Conchae They are two in number and form part of the lateral wall of the nasal cavity. They project into the nasal cavity below the middle concha. Each bone is scroll-shaped.

(g) Mandible The mandible forms the lower jaw. It is the only movable bone of the skull. It originates as two parts which unite at the midline. The upper border is also known as the **alveolar arch**: it lodges the lower teeth. The lower border or base is rounded. The middle point of the base is called the mental protuberance—chin or the **gnathion**. A ramus projects upwards almost at right angles to the posterior end of the body. The point where the ramus joins the body is the angle of the jaw.

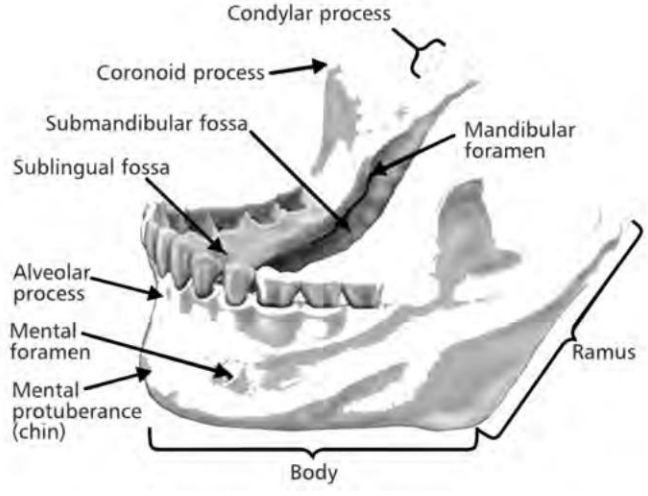


Fig. 5.8 *Mandible*

The ramus at its upper part divides into two processes. The condylar process—one on each side—which articulates with the temporal bone to form the temporo-mandibular joint and the coronoid process which gives attachment to muscles and ligaments.

The anterior surface of the body has the **symphysis menti**, the **mental protuberance** and the **mental tubercles** anteriorly. There is the mental foramen between the two molar teeth which transmit the mental nerve and vessels.

(h) Vomer The vomer is a thin flat bone. It extends from the middle of the hard palate upwards to form the main part of the nasal septum. It articulates with the perpendicular plate of the ethmoid bone.

5.1.6 Cranial Cavity

The cranial cavity or intracranial space is the space formed inside the skull. It contains the brain and meninges. There are three meninges:

1. Outer — dura mater
2. Middle — arachnoid mater
3. Inner — pia mater

The **dura mater** is the outermost, thickest and toughest membrane covering the brain. It has two layers, an outer or **endosteal layer** covering the skull and an inner or **meningeal layer** which surrounds the brain. The dura and arachnoid meninges are separated by a potential space. The arachnoid and **pia mater** are separated by a space called the **sub-arachoid space**. This space is filled with a fluid called the **cerebrospinal fluid**.

Eight fused cranial bones together form the cranial cavity: the frontal, occipital, sphenoid and ethmoid bones and two each of the parietal and temporal bones.

The capacity of an adult human cranial cavity is 1,200–1,700 cm^3.

Besides the brain and meninges, the cranial cavity also contains pineal and hypophysis-cerebri, parts of the cranial and spinal nerves, blood vessels and CerebroSpinal Fluid (CSF).

Divisions of the Cranial Cavity

The cranial cavity is divided into three subdivisions, also known as **fossae**: anterior, middle and posterior.

(a) Anterior Cranial Fossae The anterior cranial fossa accommodates the anterior lobe of the brain. It is bounded anteriorly and laterally by the frontal bone, posteriorly by the posterior border of the lesser wing of sphenoid, anterior clinoid process and the anterior margin of the sulcus chiasmatis.

The floor is formed by the orbital plate of the frontal bone, cribriform plate of the ethmoid bone and the lesser wing of sphenoid.

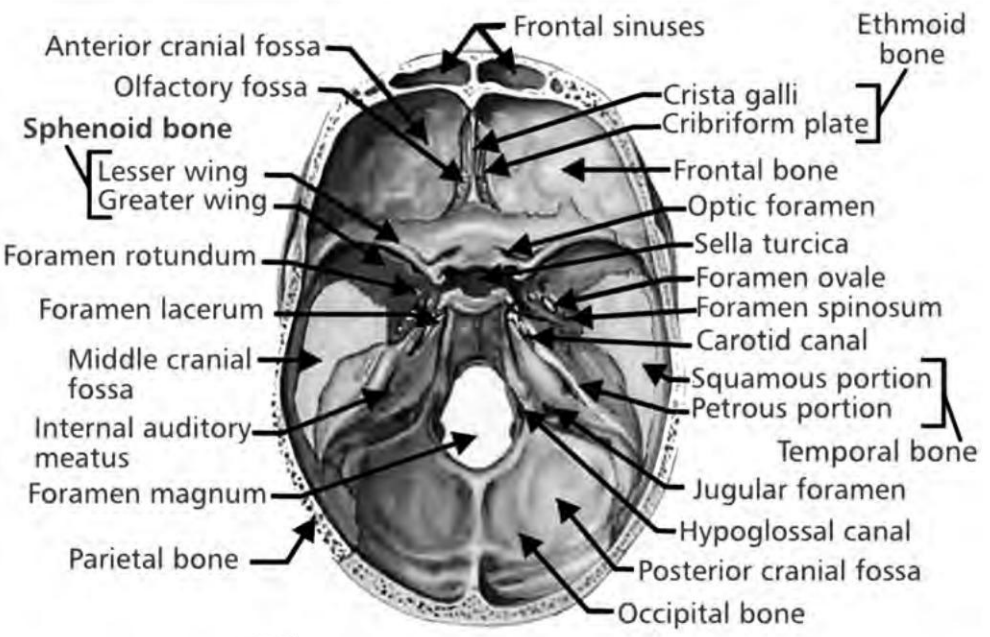


Fig. 5.9 *Cranial fossae (Refer colour figure)*

Applied Anatomy **Crista galli** is a sharp projection of the ethmoid bone. **Foramen cecum** is a small opening which lies between the crista galli and the crest of the frontal bone and which, in 85%, is closed. In 15%, it is open and communicates with the superior sagittal sinus. Infection can travel easily from the nose to this venous sinus.

There are small perforations in the cribriform plate through which pass the fibers of the olfactory nerve. If the cribriform plate is injured then there will be a loss of sensation of smell.

The orbital part of the frontal bone not only forms the floor of anterior cranial fossa but also the roof of the orbit. If injury occurs to this plate then bleeding from eye or into the eye could occur.

(b) Middle Cranial Fossa The middle cranial fossa is much deeper and wider than the anterior cranial fossa. It is shaped like a butterfly. It contains the two temporal lobes of the brain.

It is bounded anteriorly by the posterior border of the lesser wing of sphenoid, anterior clinoid process and anterior margin of sulcus chiasmatis. Posteriorly lies the superior border of petrous temporal bone and dorsum sellae of the sphenoid. The floor is formed by the body of the sphenoid bone, while situated laterally are the greater wing of sphenoid, parietal bone and squamous temporal bone.

Applied Anatomy Fracture of middle cranial fossa leads to bleeding and discharge of CSF from the ear, bleeding from nose or mouth, vertigo and damage to 7th and 8th cranial nerves.

(c) Posterior Cranial Fossa The posterior cranial fossa is the largest and deepest of the three cranial fossae.It accommodates the occipital lobes of the brain, the cerebellum, pons and medulla.

It is bounded anteriorly by superior border of petrous temporal bone, and dorsum sellae of the sphenoid bone. Posteriorly lies the squamous part of the occipital bone. The floor is formed by clivus, foramen magnum, squamous occipital, mastoid temporal bone, petrous temporal bone and mastoid angle of the parietal bone.

Applied Anatomy Fracture of posterior cranial fossa can lead to reddish discoloration of the mastoid region. It would result in difficulty in walking due to ataxia and paralysis of lower cranial nerves.

5.1.7 Vertebral Column

The vertebral column is also known as the backbone or spine. It consists of 24 separate irregular bones, viz., vertebrae, sacrum, coccyx and the intervertebral discs. The vertebral column is situated in the dorsal aspect of the torso. It houses the spinal cord in the spinal canal.

The 24 bones are grouped as

- 7 cervical
- 12 thoracic
- 5 lumbar

The sacrum and coccyx are fused bones. The sacrum consists of five fused bones, and the coccyx is made of four (3 to 5) fused bones.

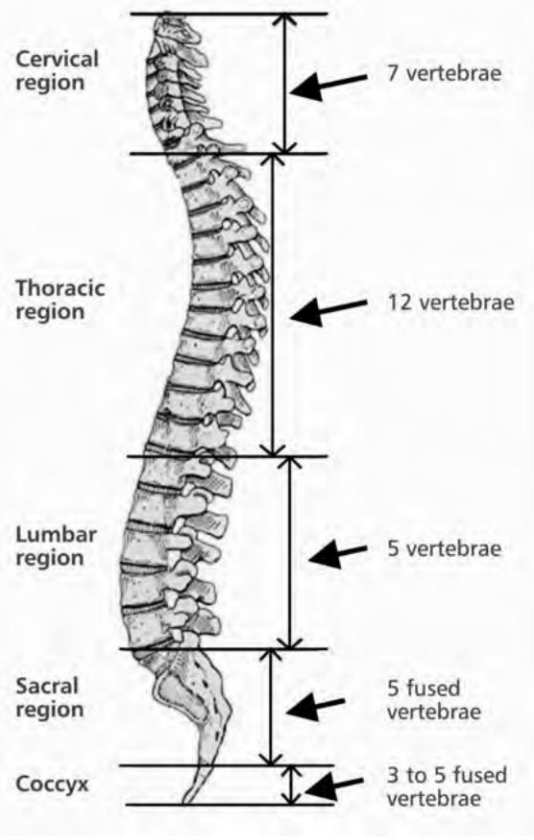


Fig. 5.10 *Vertebral column or rachis (profile view)*

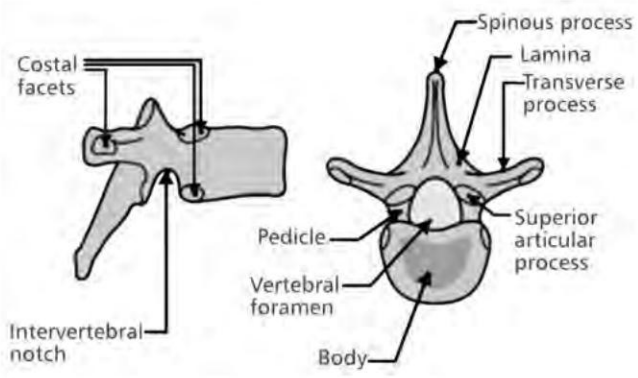


Fig. 5.11 *Typical vertebra*

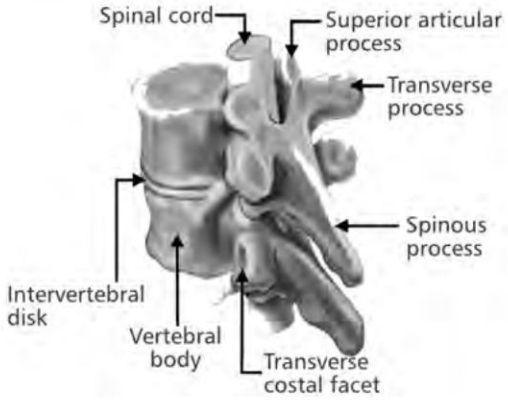


Fig. 5.12 *Typical thoracic vertebral joint*

The vertebral column presents certain curves, which correspond to different regions and are called cervical, thoracic, lumbar and pelvic curves.

A vertebra is an individual irregular bone in the spinal or vertebral column.

With the exception of the first and second cervical, the true or movable vertebrae present certain common characteristics, which are best studied by examining one from the middle of the thoracic region.

Characteristics of a Typical Vertebra

A typical vertebra consists of two essential parts:

An anterior segment, which is the vertebral body and a posterior part which is called the vertebral (neural) arch. (See Fig. 5.11)

The vertebral arch encloses the **vertebral foramen**. The vertebral arch is formed by a pair of pedicles and a pair of laminae. Where the pedicles and laminae unite, transverse processes project laterally, one on each side. The two laminae unite posteriorly to form a spinous process. The spinous processes of the cervical and lumbar regions can be felt through the skin. There are four articular surfaces on the neural arch—two articulate with the vertebrae above and two with the one below.

When the vertebrae are articulated with each other, the bodies form a strong pillar for the support of the head and trunk. The vertebral foramina constitute a canal which contains the spinal cord. In between every pair of vertebrae are two apertures, the intervertebral foramina, one on either side, for the transmission of the spinal nerves and vessels.

Special Features in the Different Vertebrae

(a) Cervical Vertebrae The body is small and broader from side to side than anteroposteriorly (i.e., from front to back). The superior surface is concave transversely with projecting lips on each side. The inferior surface is convex from side to side and concave anteroposteriorly. The lateral borders are beveled and form synovial joints with the projecting lips of the next lower vertebra. The transverse processes have a foramen through which a vertebral artery passes upwards to the brain.

The first two cervical vertebrae are atypical.

The first cervical vertebra is called the **atlas**. It is ring-shaped and has no body and no spine. It has a short anterior arch, a long posterior arch, right and left lateral masses and two short transverse processes. The anterior arch on its anterior aspect has a median anterior tubercle.

The posterior arch is longer than the anterior arch and forms two fifths of the ring. Its posterior surface is marked by a median posterior tubercle.

The lateral mass has the superior articular facet which articulates with the corresponding condyle to form the **atlantooccipital joint**. The inferior articular facet on the inferior surface, articulates with the corresponding facet on the axis (the second cervical vertebra) to form the **atlantoaxial joint**. The medial surface of the lateral mass is marked by a small roughened tubercle.

The anterior part of the vertebral foramen is occupied by the odontoid process of the axis and thus it takes the place of the body of the atlas. The posterior part is the true vertebral foramen and is occupied by the spinal cord.

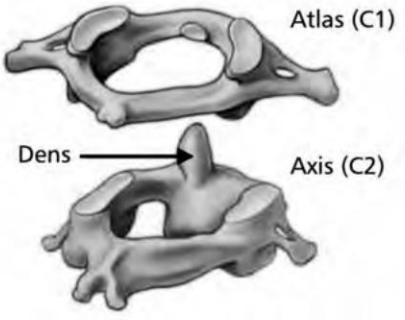


Fig. 5.13 *Cervical vertebrae*

The transverse process projects laterally from the lateral mass. It is long and can be felt on the surface of the neck between the angle of the mandible and the mastoid process. This long length acts as a lever to allow rotatory movements of the head.

The second cervical vertebra is called the **axis**. It is identified by the upward projecting odontoid process or dens which is a strong, toothlike process. The dens is usually believed to represent the body of the atlas which has fused with the centrum of the axis. The laminae are thick and strong. The transverse processes are small. The spine is large, thick and strong. Its main function is to allow movement at this joint, to turn the head from side to side.

(b) Thoracic Vertebrae The thoracic vertebrae are identified by the presence of costal facets on the sides of the vertebral bodies.

There are twelve thoracic vertebrae, out of which 2nd to 8th is typical. The 1st, 9th, 10th, 11th and 12th are atypical. The upper four, middle four and lower four are called upper, middle and lower dorsal vertebrae respectively.

Its body is heart-shaped. It has 2 costal facets on either side. The superior costal facets are larger and articulate with the head of the numerically corresponding rib. The inferior costal facets are smaller and articulate with the next lower rib.

The pedicles are directed straight backwards. The laminae overlap each other from above. The superior articular processes project upwards from the junction of the pedicles and laminae. The inferior articular processes are fused to the laminae. The transverse processes are large and are directed backwards and laterally. The spinous process is long and directed backwards and downwards.

The body of the first thoracic vertebra resembles that of a cervical vertebra. It is not heart-shaped. The spine is thick, long and nearly horizontal. The superior vertebral notches are well marked.

The ninth thoracic vertebra is a typical thoracic vertebra but the body has only the superior costal facets. The inferior costal facets are absent.

The tenth thoracic vertebra resembles a typical thoracic vertebra except that the body has a single complete superior costal facet on each side which extends to the root of the pedicle.

The eleventh thoracic vertebra has a single large costal facet on either side which extends to the upper part of the pedicle. The transverse process is small and has no articular facet.

The twelfth thoracic vertebra has the characteristics of a lumbar vertebra. The shape of the body, pedicles, spine and transverse processes are similar to those of a lumbar vertebra. There is a single costal facet on each side. The transverse process is small. The superior articular facet is thoracic in type while the inferior articular facet is lumbar in type.

(c) Lumbar Vertebrae All the features are as in a typical vertebra. There are no special features.

(d) Sacrum and Coccyx The sacrum and coccyx are commonly referred to as 'base bone' or 'tail bone'. The sacrum consists of five individual bones and the coccyx is made up of three to five bones in childhood. In the adult, the sacral segments and the coccygeal segments fuse so that each of these two bones is a solid singular bone.

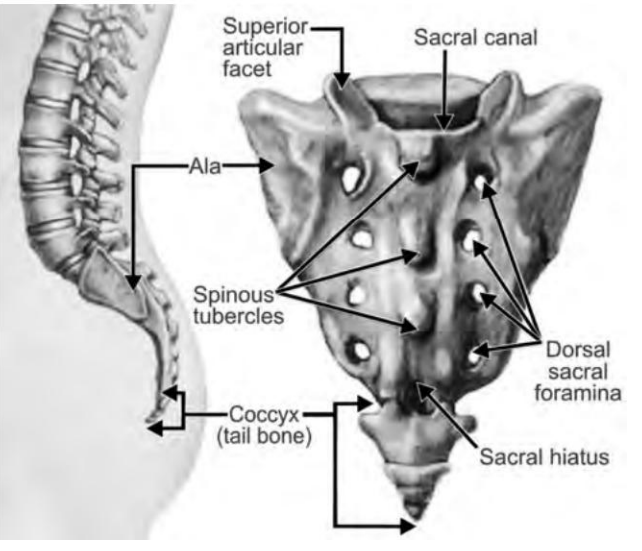


Fig. 5.14 *Sacrum and coccyx*

The sacrum forms joints with each of the hip bones and helps to stabilize the pelvis. It forms a triangular or wedge-shaped bone with a concave anterior surface. The upper part is called the base and articulates with the 5th lumbar vertebra. The tip articulates with the coccyx. The anterior edge of the base is called the **promontory**. It protrudes into the pelvic cavity. The vertebral foramina are present on either side of the bone and allow passage of nerves.

The coccyx has a broad base which articulates with the tip of the sacrum.

Functions of the Vertebral Column

1. The main function of the vertebral column is to allow humans to stand upright and maintain their balance.
2. It helps to support the head and arms.
3. All the vertebral foramina jointly form a vertebral canal. This gives a good bony protection to the spinal cord.
4. It also provides attachment for many muscles and ribs.
5. The intervertebral foramina are formed by the pedicles of adjacent vertebrae. This allows passage of spinal nerves, blood vessels and lymph vessels.
6. It protects the brain. This is due to the intervertebral discs which act as shock absorbers.
7. It forms the axis of the trunk.

5.1.8 Thoracic Cage

The thoracic cage, also called the rib cage, as the name suggests, is the cagelike structure formed by the thoracic vertebrae, ribs, the sternum and the costal cartilages, that attach the ribs to the sternum.

1. Sternum

The sternum is a flat bone which can be felt under the skin in the middle of the front of the chest.

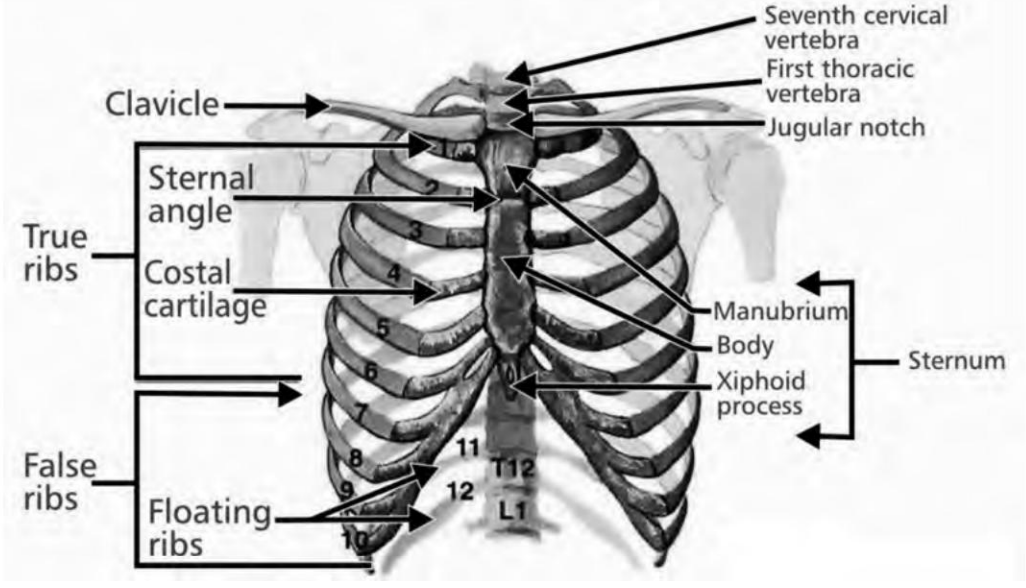


Fig. 5.15 *Thoracic cage*

The sternum is formed by the manubrium, body and xiphisternum. The **manubrium** is notched on its upper (superior) margin forming the jugular notch. It articulates with the clavicles and forms the sternoclavicular joint. The first rib articulates immediately below the sternoclavicular joints. The second rib articulates at the manubriosternal joint.

The body of the sternum gives attachment to the ribs.

The tip of the sternum is called the **xiphoid process**. It gives attachment to the diaphragm, the anterior abdominal muscles and the linea alba.

2. Ribs

There are 12 pairs of ribs. They form the anterior, posterior and lateral wall of the thoracic cage. The upper seven ribs articulate anteriorly directly with the sternum through their costal cartilages and are called true ribs. The lower 5 ribs are called false ribs of which 8th, 9th and 10th ribs join the sternum through a fused cartilage while the 11th and 12th ribs do not articulate anteriorly and, therefore, are called floating ribs.

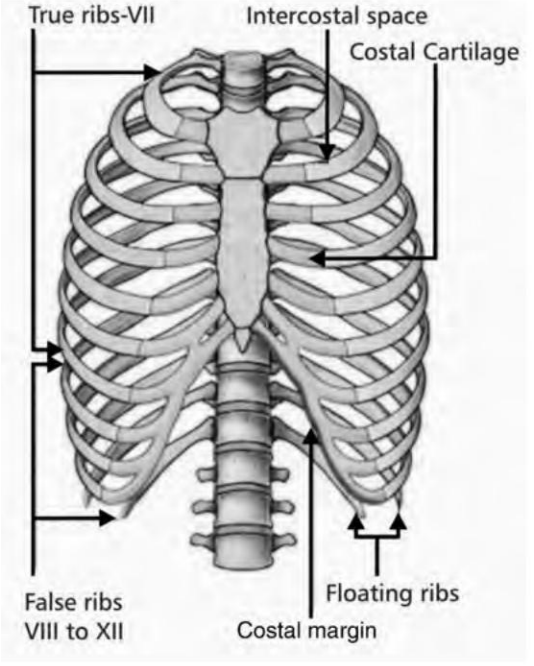


Fig. 5.16 *Ribs*

The first rib is flattened above and below. Its anterior cartilage is fused to the manubrium forming a rigid ring, the thoracic inlet. During respiration, the thoracic inlet is fixed. The second to seventh ribs articulate anteriorly with the sternum through synovial joints.

Posteriorly, the ribs articulate with the thoracic vertebrae. The head articulates with the bodies of two adjacent vertebrae. The tubercle of a typical rib articulates with the facets on the tip of the transverse process of its own vertebra to form a synovial joint.

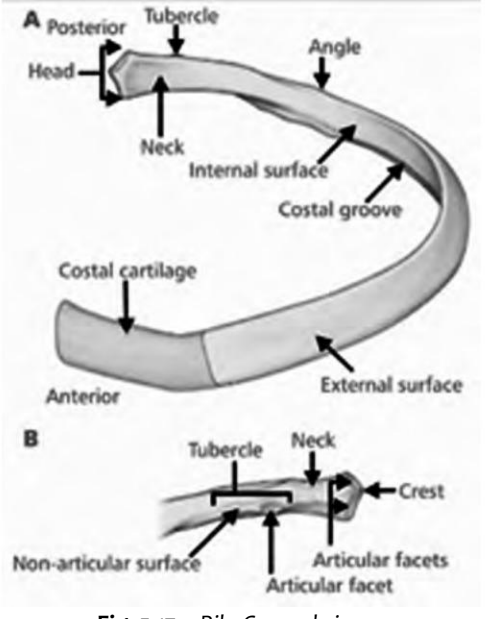


Fig. 5.17 *Rib: General view*

These articulations allow the ribs to move upwards and outwards during inspiration, so increasing the anterior–posterior and side–to–side diameters of the thorax. These movements are called pump-handle and bucket-handle movements. This increases the thoracic diameters because of the downward slant of the rib and due to its curvature.

5.1.9 Appendicular Skeleton

The appendicular skeleton consists of the bones of the upper limbs with the shoulder girdle and the bones of the lower limbs with the pelvic girdle.

1. Shoulder Girdle and Upper Limb

The shoulder girdle connects the upper limb to the axial skeleton on each side. It consists of the clavicle and scapula.

2. Clavicle

The clavicle or the collar bone is a double-curve shaped bone. It keeps the scapula in position so that the arm can hang freely. It is located directly above the first rib. It has a rounded medial end and a flattened lateral end. Medially, it articulates with the manubrium of the sternum at the sternoclavicular joint. Laterally, it articulates with the acromion of the scapula forming the acromio-clavicular joint.

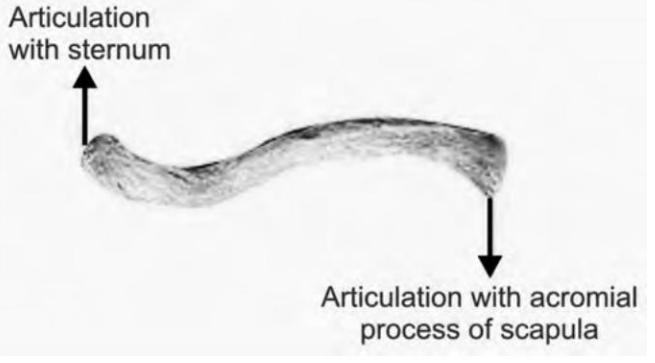


Fig. 5.18 *Clavicle*

Clavicular fractures are very common. It usually breaks at the junction of the two curves.

3. Scapula

The scapula is the bone that connects the humerus with the clavicle. It forms the posterior part of the shoulder girdle. It is a flat bone, roughly triangular in shape and covers parts of 2^{nd} to 7^{th} ribs.

It has a concave costal or anterior surface called the **subscapular fossa** and a convex posterior surface from which the spine projects dividing it into unequal parts—smaller upper supraspinous fossa and larger lower infraspinous fossa.

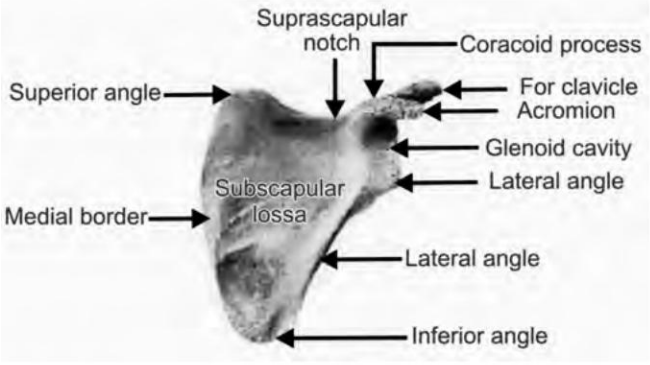


Fig. 5.19 *Scapula*

The spine continues laterally into a flattened process called the **acromion**. It projects anteriorly and articulates with the clavicle at the acromio-clavicular joint.

There is a projection supero-anteriorly, arising from the upper border called the **coracoid process**, which gives attachment to the muscles that move the shoulder joint.

It has a shallow articular surface called the **glenoid fossa** or **glenoid cavity** at the lateral angle of the scapula where the head of humerus articulates to form the shoulder joint.

The scapular notch is in the superior border.

The scapula contributes to the wide range of movement of the upper limb.

4. Humerus

The humerus is a long bone in the upper arm, situated between the shoulder and elbow. It connects the scapula and the lower arm. The upper end consists of a rounded head, a narrow neck and two short processes or tubercles—**greater tuberosity** and **lesser tuberosity**. The head articulates with the glenoid fossa of the scapula. The body is cylindrical in its upper portion, is flat at lower end and is prism-shaped.

The lower end consists of two epicondyles, two processes—**trochlea** and **capitulum**, and three fossae—**radial fossa**, **corocoid fossa** and **olecranon fossa**. When the elbow is flexed, the coronoid process of the ulna fits into the corocoid fossa and when the elbow is extended, the olecranon process of the ulna fits into the olecranon fossa.

More distally, at the elbow, there is a rounded convex projection laterally called the capitulum, which articulates with the head of the radius. On the medial side there is a pulley-shaped surface called the **trochlea** which articulates with the olecranon process of the ulna. (See Fig. 5.20)

5. Radius

The radius is a long bone of the forearm that extends from the elbow to the thumb side of the wrist and lies on the lateral side of the ulna. It has an upper end, a lower end and a shaft. It is prismatic in form and slightly curved longitudinally.

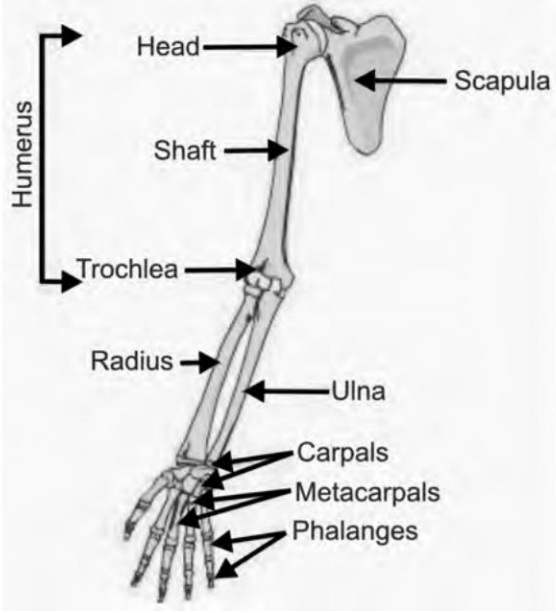


Fig. 5.20 *Bones of the upper limb*

The upper end is small and has a head, neck and tuberosity. It forms only a part of the elbow joint. The head is of a cylindrical form and has on its upper surface a shallow cup or fovea, for articulation with the capitulum of the humerus. The head is supported on a round constricted portion called the neck. It articulates with the radial notch of the ulna. On the medial side, below the neck is a prominence called the **radial tuberosity**. The body has three borders and three surfaces; the lower end is large, quadrilateral in form and has two articular surfaces. The one on the medial side articulates with the ulna and the one below articulates with the carpus. At the lateral end there is a downward projection called the **styloid process**.

6. Ulna

The ulna is a long bone placed on the medial side of the forearm and is slightly longer than the radius. It is prismatic in form and is broader proximally and narrower distally.

It has a shaft, upper and lower extremities. The upper end has a bony process, the olecranon process, a hooklike structure which fits into the olecranon fossa of the humerus. Adjacent to it is a C-shaped cavity called the **trochlear notch** which forms a hinge joint with the trochlea of the humerus. The floor of this notch projects forwards in a process called the **corocoid process**. There is also a radial notch for the head of the radius and forms a pivot joint with it, which allows the radius to cross the ulna in pronation. The shaft becomes thinner downwards. The lower end again expands to form the head. Medially, at the distal end, there is a process called the **styloid process**. The distal end fits into the ulnar notch.

7. Bones of the Wrist and Hand

The hand consists of 27 bones—the carpus or wrist has 8 bones; the palm contains 5 and the remaining 14 are the bones of fingers and thumb.

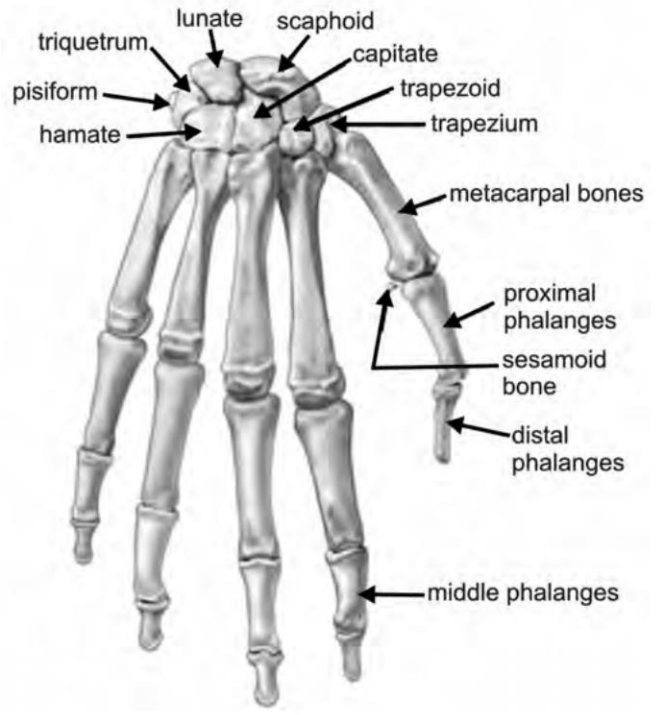


Fig. 5.21 *Bones of the wrist and hand*

The eight bones of the wrist, also called **carpal bones**, are arranged in two rows of four—four proximal and four distal. They are irregularly shaped. They fit into the shallow socket formed by the lower ends of the bones of the forearm. The bones of the proximal row are scaphoid, lunate, triquetral and pisiform. The bones of the distal row are trapezium, trapezoid, capitate and hamate.

The palm has five bones called the **metacarpal bones**, one to each of the five digits. They have a base, a shaft and a head. The bases articulate with the distal row of carpal bones and the heads articulate with the proximal row of phalanges.

There are fourteen **phalanges**. Three in each of the four fingers—proximal, middle, distal and two in the thumb (no middle phalanx).

The articulations in the hand are interphalangeal articulations of hand, metacarpophalangeal joints, intercarpal joints and articulation with the bones of the forearm.

5.1.10 Hip and Lower Limb

1. Hip Bone

The hip bone is a large, flattened, irregularly shaped bone which is constricted in the center and expanded above and below. It meets its component of the other side in the middle in front and together they form the sides and anterior wall of the pelvic cavity.

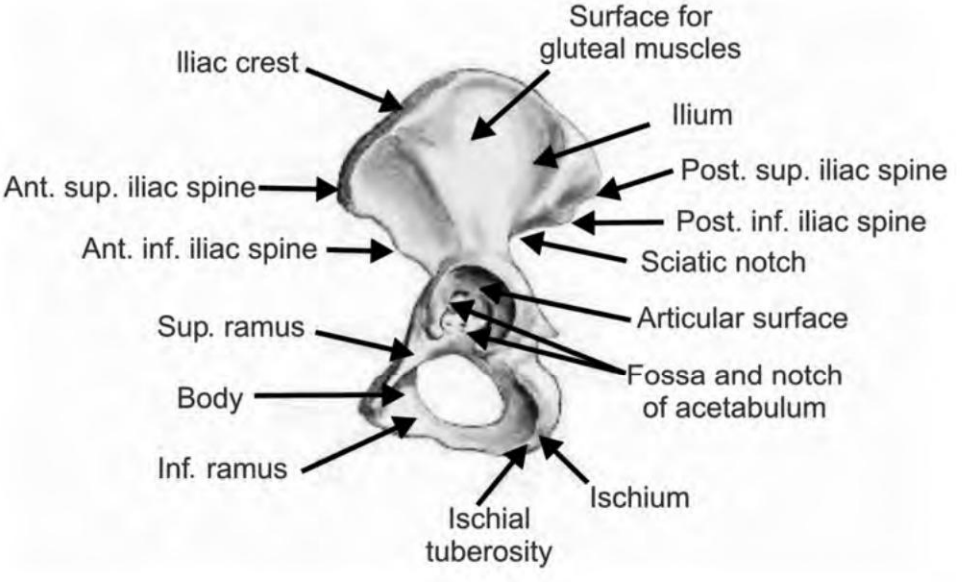


Fig. 5.22 *Hip bone*

It consists of the three bones—ileum, ischium and pubis, which is distinct from each other in the young age and in the adult, is fused. The union of these three bones takes place in and around a large cup-shaped articular cavity, called the **acetabulum**, situated on the outer side.

The **ileum** is the upper broad and expanded portion extending upwards from the acetabulum. The **ischium** goes downwards from the acetabulum and is the lowest and strongest part. It expands into a large tuberosity, curves upwards and forms a large aperture with the pubis, called the **obturator foreman**.

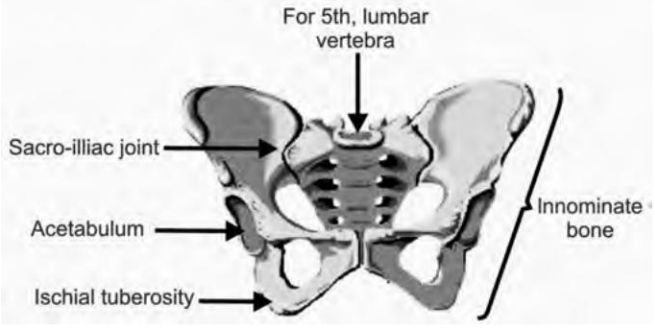


Fig. 5.23 *Pelvis*

The pubis articulates with the bone of the opposite side at the pubic symphysis.

Together with head of femur it forms the ball and socket joint—hip joint.

With the sacrum and coccyx, the hip bone comprises the pelvis which supports and accommodates the organs of the abdomen like urinary bladder, uterus, etc.

The pelvis of males and females differ in size, shape and angles. This is due to the needs of the female associated with pregnancy and childbirth.

Table 5.1 *Differences between male and female pelvis*

Male	*Female*
Narrower	Wider
Deeper	Shallower
Sacrum—narrower and longer	Sacrum—wider and shorter
Pubic arch forms acute angle	Pubic arch forms obtuse angle
Muscle attachment deeper	Muscle attachment shallower

2. Femur

The femur is the largest and strongest bone of the body and is situated between the pelvis and the knee. It has a body and two extremities. It is compared to the humerus of the upper limb. The upper end has a round head which articulates with the acetabulum of the hip bone and forms the ball-and-socket joint. It also has a neck, and a greater and lesser trochanter. The acetabulum is deeper than the glenoid cavity.

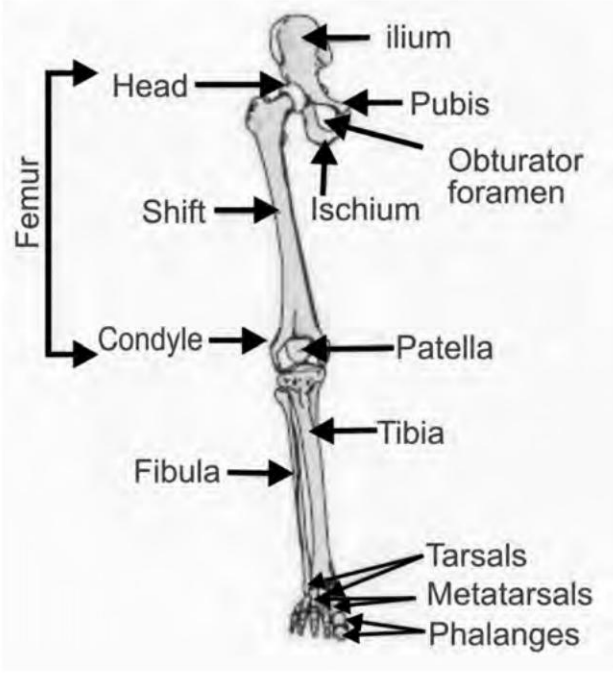


Fig. 5.24 *Bones of the lower limb*

The neck is a flattened pyramidal process connecting the head to the body. The **greater trochanter** is a large irregular quadrilateral eminence, situated at the junction of the neck with the upper part of the body. The **lesser trochanter** is a conical eminence projecting from the lower and back part of the base of the neck.

The body is cylindrical in form and broad at the upper part. It has three borders separating the three surfaces. The posterior surface of the lower third forms a flat triangular area called the **popliteal surface**. The lower end is larger than the upper part, cuboidal in form and has two oblong eminences known as the condyles. The **condyles** with the tibia and patella form the knee joint.

3. Tibia

The tibia is the inner and larger bone of the leg below the knee. The upper end is broad and flat and has two condyles which articulate with the femur. The head of the fibula articulates with the inferior aspect of the lateral condyle.

The lower end has a projection called the **medial malleolus**, which is medial to the ankle joint. This lower end forms the ankle joint with the talus and fibula.

4. Fibula

The fibula is located on the lateral side of the tibia and is long and slender. It is attached to the tibia at both the ends. The upper end articulates with the lateral condyle of the tibia and forms the **proximal tibiofibular joint**. The lower end articulates with

the tibia to form the **distal tibiofibular joint** and then projects downwards to form the **lateral condyle**.

While the tibia performs the function of weight bearing, the fibula only gives attachment to muscles.

5. Patella

The patella is a mobile roughly triangular-shaped bone forming the knee cap. The posterior surface articulates with the patellar surface of the femur in the knee joint. The anterior surface lies in the patellar tendon.

6. Bones of the Foot

There are 26 bones in each foot and 2 sesamoid bones.

There are 7 **tarsal** bones arranged in two rows that form the posterior part of the foot. They are 1 talus, 1 calcaneus, 1 navicular, 3 cuneiform and 1 cuboid.

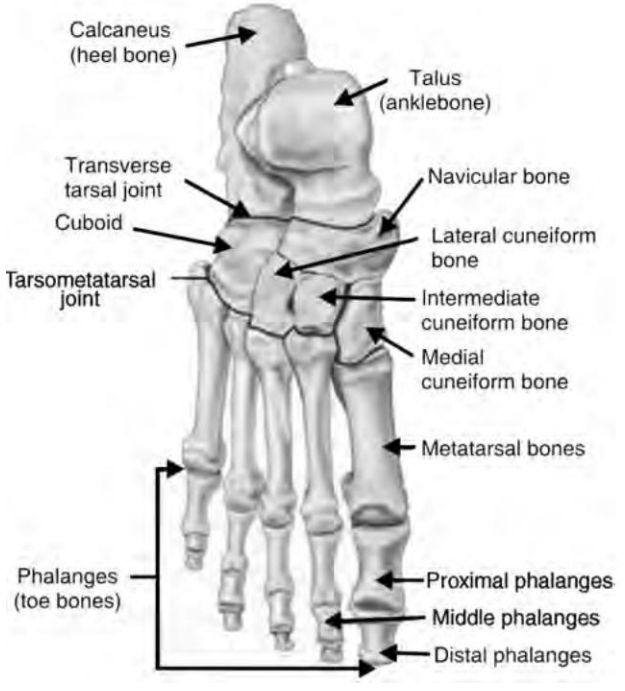


Fig. 5.25 *Bones of the foot*

They help to bear the weight of the body. The **talus** articulates with the tibia and fibula at the ankle joint. The calcaneus forms the heel while the rest articulate with one another and with the metatarsal bones.

There are five **metatarsal** bones which form the greater part of the dorsum of the foot. They articulate with the tarsal bones at the proximal end and with the phalanges at the distal end. The ball of the foot is formed by the enlarged distal head of the first metatarsal bone.

There are 14 **phalanges**—12 for 4 toes and 2 for the great toe—proximal, middle and distal, middle absent in the great toe.

Two sesamoid bones are present in the tendons of the flexor hallucis brevis.

7. Arches of the Foot

The foot has two functions to perform—weight bearing and movement. Hence, it requires a high degree of stability. The bones and joints give it flexibility but to bear weight, the bones need to form an arch.

The arches are formed by the tarsal and metatarsal bones strengthened by tendons and ligaments. There are four arches—medial and lateral longitudinal arches and two transverse arches.

The **medial arch** is formed by the calcaneus, the talus, the navicular, three cuneiform and the first three metatarsal bones. This is the highest of the arches. The calcaneus and distal end of the metatarsal bones only should touch the ground.

The **lateral arch** is formed by the calcaneus, the cuboid and the two lateral metatarsal bones. The calcaneus and distal end of the metatarsal bones only should touch the ground. It is less marked than the medial arch.

Two **transverse arches** run across the foot. They are most marked at the level of the three cuneiform and cuboid bones.

5.1.11 Disorders of Bones

1. Osteoporosis

Osteoporosis is a condition in which the amount of bone tissue is reduced and the strength of the trabecular bone is decreased. Deposition does not keep pace with absorption. It weakens the bone and there is an increased risk of the development of fracture.

Pathophysiology Osteoporosis mostly occurs in older people and in women after menopause. After menopause, for a certain period of time, there is loss of bone mass in females as they stop producing oestrogen, a bone-protecting hormone. After that period, in both sexes, there is imbalance of hormones between anabolic steroids (estrogen and androgens) and glucocorticoids, which is an anti-anabolic steroid.

Many disorders are associated with increased risk of osteoporosis like endocrine disorders, nutritional deficiencies, drugs and hematological disorders.

Certain risk factors and environmental factors are associated with decrease in the bone mass and development of osteoporosis, e.g., gender, race, diet, lifestyle, and lack of sunlight.

Calcium and exercise play an important role in determining bone mass. Hence, decreased calcium intake and sedentary life decreases bone mass.

Immobility of a limb, e.g., in an unconscious person or in a fractured limb, also leads to osteoporosis which is reversible.

2. Osteomalacia

In osteomalacia, there is softening of bones. In children, it is called rickets and in adults it occurs after ossification is complete. In children, osteoid gets deposited but calcification is not complete and bones remain soft. In the lower limbs it leads to bowing. In adults, there is increased and abnormal turnover of bone and osteoid is not calcified. Bones get soft, bowed and fractured.

Pathophysiology Deficiency of vitamin D is the chief causative factor. It promotes absorption of calcium from the intestine and calcification of bone. Deficiency could be due to dietary deficiency or due to lack of absorption as in malabsorption syndrome. Lack of sunlight, especially in children, can cause defective production of vitamin D.

Conditions which interfere with the metabolism of vitamin D, e.g., intake of druglike anticonvulsants, can cause osteoporosis.

Excessive loss of the vitamin, e.g., in renal failure, leads to osteoporosis.

3. Osteomyelitis

Osteomyelitis is the bacterial infection of the bone, usually spread through blood. The most common is *Staphylococcus aureus* infection. Infection of the bone is followed by inflammation which could resolve or if untreated may proceed to bone necrosis, suppuration, spread to surrounding soft tissue and joint. There may result a periosteal abscess which could rupture through the skin forming a sinus and this becomes chronic.

Pathophysiology Bone infections can occur at any age. Bacteria can reach the bone through a compound fracture, through blood from a boil or infection of soft tissue anywhere in the body, or during a surgical procedure.

Certain conditions like diabetes, sickle-cell anemia, a foreign body in the bone, e.g., bullet, or drug abuse (heroin), increase the risk of developing infection.

4. Paget's Disease

Paget's disease of the bone is a chronic bone disorder which can affect one bone, part of bone or many bones. Osteoblasts and osteoclasts become overactive in some areas of bone and deposit abnormal new bone. These overactive areas enlarge but are structurally abnormal and hence weaker than normal bone. This leads to deformities and as they are fragile, fractures are common.

Pathophysiology The cause is not known. Age and heredity are the only known risk factors.

5. Achondroplasia

Achondroplasia is a congenital disease. The affected person has abnormally short stature with disproportionately short limbs. The defect is not in the formation of cartilage but there is abnormal growth of cartilage and it is not converted into bone, particularly the long bones. This leads to dwarfism. The bones of the base of the skull are also under-developed.

5.2 JOINTS

A joint is the location at which two or more bones articulate or make contact. Some joints like those of the skull are fixed and have no movement, some like those of the vertebrae can move slightly and some are freely moveable like the joints of the limbs.

5.2.1 Classification of Joints

Joints are classified into

1. Fibrous, or fixed joints
2. Cartilaginous, or slightly movable joints
3. Synovial, or freely movable joints

1. Fibrous Joints or Fixed Joints

Fibrous joints connect bones without allowing any movement. The bones of the skull and pelvis are held together by fibrous joints. The union of the spinous processes and vertebrae, joints between the teeth and maxilla and mandible are examples of fibrous joints.

2. Cartilaginous, or Slightly Movable Joints

Cartilaginous joints are joints in which the bones are attached by cartilage. In this type of joint, there is a pad of fibrocartilage between the ends of bones which form joints, where only some movement is required. Joints at the pubic symphysis, the joint between the manubrium sterni and body of the sternum, and joints between the vertebral bodies are examples of cartilaginous joints.

3. Synovial, or Freely Movable Joints

Synovial joints allow far much more movement than cartilaginous joints. They have a layer of hyaline cartilage on the bones which are in contact with each other. This cartilage covering is normally 7-mm thick and becomes thinner with age. It absorbs forces and bears the weight of the body. Cavities between bones in synovial joints are filled with synovial fluid which helps lubricate and protect the bones. Cartilage gets its nourishment from the synovial fluid.

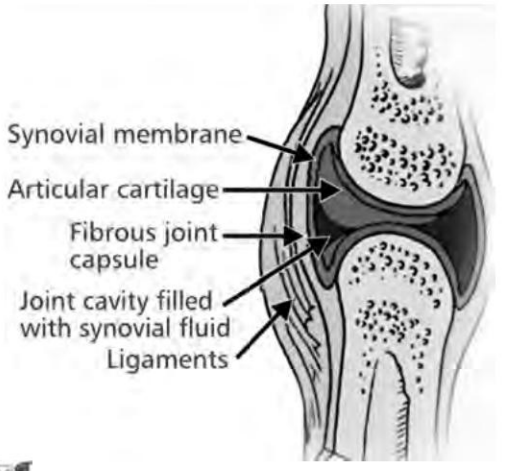


Fig. 5.26 *Synovial joint (Refer colour figure)*

These joints have a covering of fibrous tissue which protects the joint from injury and is loose enough to allow free joint movement. This is called **capsule of the joint.**

Inside the capsule is a layer of epithelial cells which forms the synovial membrane. This membrane covers those parts of the bones which are not covered by cartilage and those structures inside the capsule which do not bear weight.

Synovial joints allow a wide range of movements. They are further classified depending on the range of movements and shape of articular parts.

Characteristics of Synovial Joints

1. The joint is enclosed and surrounded by fibrous tissue. This keeps the bones together. The capsule is such that it protects the bones and joint from injury and at the same time allows free movement.
2. The bones which form the joint and which are in contact with each other are covered with hyaline cartilage, called **articular cartilage**. Hence, the articular surfaces are smooth. The hyaline cartilage also bears the weight of the body. It reduces friction of the joint. As age advances, the cartilage becomes thinner. This causes stress on the other structures in the joint. The hyaline cartilage gets its nourishment directly from the synovial fluid.
3. The synovial membrane lines the capsule, covers all the intracapsular structures and also covers those parts of the bones within the joints which are not covered by the articular cartilage. It consists of epithelial cells.
4. Synovial fluid is secreted by the synovial membrane into the joint cavity. It is thick and sticky, is of egg-white consistency and acts as a lubricant.
   - It provides nutrition to the structures within the joint cavity.
   - It gives stability to the joint.
   - It acts as a seal, waterproofing the joint.
   - It contains phagocytes which remove microbes and cellular debris.
   - It keeps the ends of bones intact and prevents them from being separated.
   - In some joints, **bursae**, or small sacs of synovial fluid, are present, which prevent friction between a bone and ligament or tendon or skin.
5. In addition to the capsule, the bones are also attached and held together by strong and tough ligaments made of dense connective tissue. These ligaments prevent dislocation during normal movement.
6. The articulating surfaces of adjacent bones are reciprocally shaped.

5.2.2 Types

1. Ball-and-socket Joint

In this type of joint, the head of one bone articulates with the socket of another bone. This allows a wide range of movement. It allows for radial movement in any direction, e.g., shoulder joint and hip joint. In this joint, there is flexion, extension, adduction, abduction, internal and external rotation and circumduction.

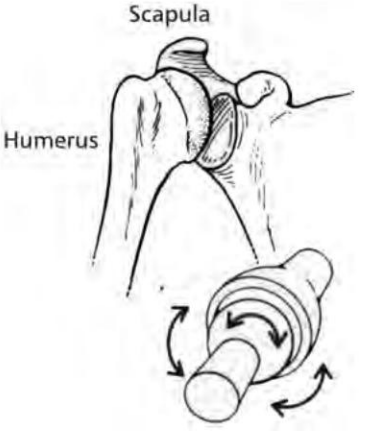


Fig. 5.27 *Ball-and-socket joint*

2. Gliding Joints

In this type of joint, the articular surfaces glide over each other, e.g., joints between carpal bones and between tarsal bones, sternoclavicular joint, and acromioclavicular joint.

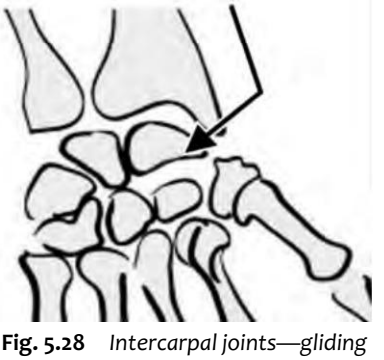


Fig. 5.28 *Intercarpal joints—gliding*

3. Hinge Joints

In this type of joint, only two movements are possible, flexion and extension, e.g., elbow, knee, ankle, interphalangeal joints of fingers and toes and the joint formed between the atlas and occipital bone.

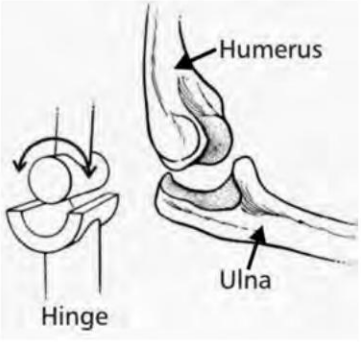


Fig. 5.29 *Hinge joints*

4. Pivot Joints

In this type of joint, the movement is in the form of rotation. The movement is around an axis. The neck and forearms have pivot joints. In the neck, the occipital bone spins over the top of the axis. In the forearm, the radius and ulna twist around each other.

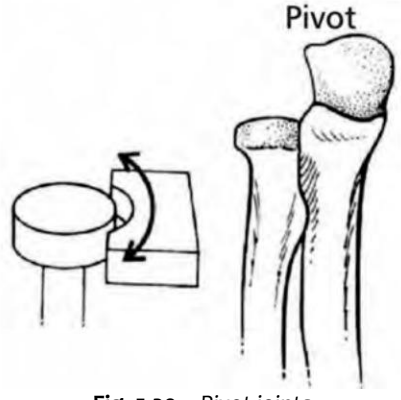


Fig. 5.30 *Pivot joints*

5. Saddle Joints and Condyloid Joints

A saddle joint allows movement back and forth and up and down, but does not allow rotation like a ball-and-socket joint.

In this type of joint, the movements take place around two axes. The movements are flexion, extension, abduction, adduction and circumduction, e.g., in the wrist joint, metacarpophalangeal and metatarsophalangeal joints and the temporomandibular joint.

All these are synovial joints and they have certain characteristics.

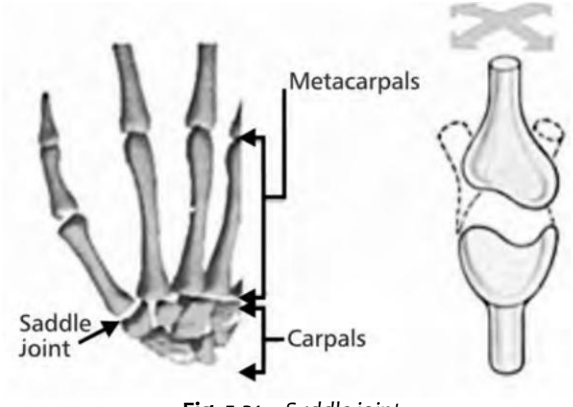


Fig. 5.31 *Saddle joint*

5.2.3 Main Synovial Joints of the Limbs

1. Upper Limbs

(a) Shoulder Joint It is a ball-and-socket type of joint. The head of the humerus rotates within the glenoid cavity of the scapula. It is also known as **humero-scapular joint**.

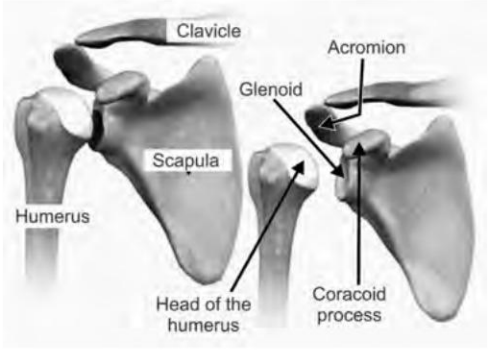


Fig. 5.32 *Shoulder joint*

(b) Elbow Joint This joint is formed by the trochlea of the humerus with the trochlear notch of the ulna and the capitulum of the humerus with the head of the radius. It is a type of hinge joint. (See Fig. 5.32)

(c) Radio-ulnar Joints—Proximal and Distal The proximal radi-o-ulnar joint is formed by the rim of the head of the radius rotating in the radial notch of the ulna and it has little movement. The distal joint is formed between the distal end of the radius and the head of the ulna. It is a pivot joint.

(d) Wrist Joint This joint is formed by the distal end of the radius and the proximal ends of the scaphoid, lunate and triquetral wrist bones. It is a condyloid joint.

(e) Joints of Wrist and Fingers These are joints between the carpal bones, between carpal and metacarpal bones and between the metacarpal bones and proximal phalanges and between the phalanges. Intercarpal and carpal–metacarpal

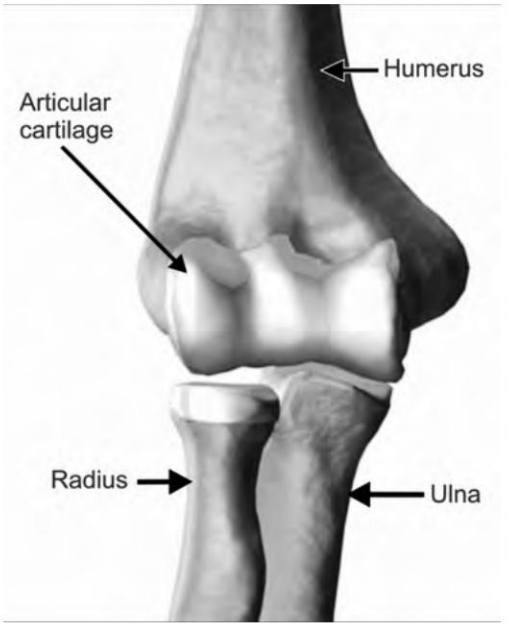


Fig. 5.33 *Elbow joint*

joints are gliding joints. Metacarpophalangeal joints are condyloid joints and interphalangeal joints are hinge joints.

2. *Lower Limbs*

(a) Hip Joint The head of the femur bone fits into the cup-shaped acetabulum of the hip bone. It is a ball-and-socket type of joint.

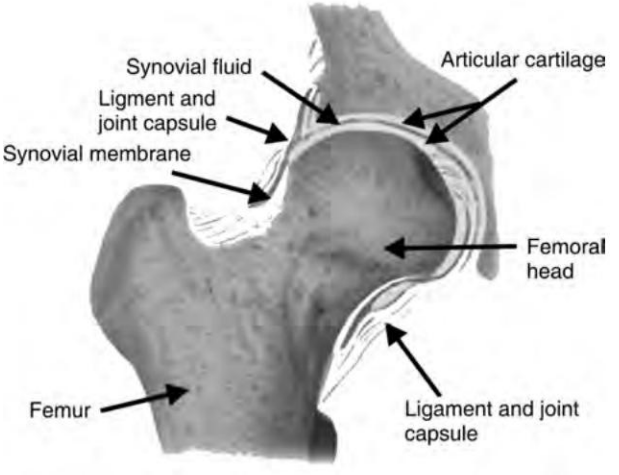


Fig. 5.34 *Hip joint*

(b) Knee Joint It is formed by the two condyles of the femur with the condyles of the tibia and the posterior surface of the patella. It is a type of hinge joint. (See Fig. 5.35)

(c) Ankle Joint This joint is formed by the distal end of the tibia and its medial malleolus, the distal end of the fibula and its lateral malleolus with the talus. It is a form of hinge joint.

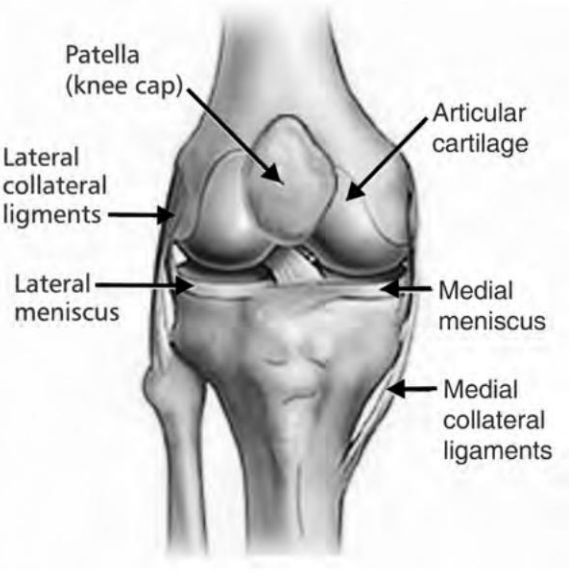


Fig. 5.35 *The right knee*

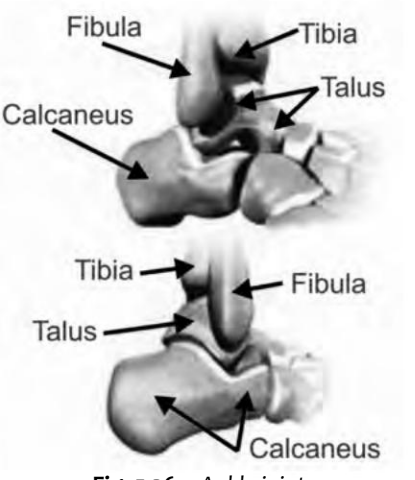


Fig. 5.36 *Ankle joint*

(d) Joints of the Foot and Toes Joints are formed between the tarsal bones, between the tarsal and the metatarsals, between the metatarsal bones and the proximal phalanges and between the phalanges. They are all gliding type of joints.

5.2.4 Joint Movements

In a healthy joint, the movement takes place in various directions depending on the type of the joints.

The movements possible in joints may be divided into four kinds, viz., gliding, angular, circumduction and rotational.

- **Gliding movement** is the simplest kind of motion. One surface glides or moves over another without any angular or rotatory movement. It is common to all movable joints. In the carpal and tarsal joints, it is the only movement seen.

- **Angular movement** occurs between the long bones. The angle between the two bones is increased or diminished. There can be forward and backward movement constituting flexion and extension; or the movement could be toward or away from the median plane of the body. In fingers or toes, the movements are adduction and abduction. Abduction and adduction, combined with flexion and extension, are seen in the hip, the shoulder, the wrist and the carpometacarpal joint of the thumb.
- **Circumduction** is the movement which takes place between the head of a bone and its articular cavity. A sort of cone is described in this movement where the base of the cone is described by the distal end of the bone; the apex is in the articular cavity. This type of movement is seen in the shoulder and the hip joints.
- **Rotation** is a movement in which a bone moves around a central axis without any displacement from this axis. The axis of rotation may lie in a separate bone, as seen in the pivot formed by the odontoid process of the axis around which the atlas turns; or a bone may rotate around its own longitudinal axis, as in the rotation of the humerus at the shoulder joint; or the axis of rotation may not be parallel to the long axis of the bone, as in the movement of the radius on the ulna during pronation and supination of the hand.

5.2.5 Disorders of Joints

1. Arthritis

Arthritis is inflammation of one or more joints resulting in pain, swelling, stiffness and limitation of movement. There are over 100 different forms of arthritis. The most common forms are osteoarthritis and rheumatoid arthritis. Other forms are psoriatic arthritis, ankylosing spondylitis, rheumatic fever and Reiter's syndrome. Septic arthritis is caused by joint infection.

2. Rheumatoid Arthritis

Rheumatoid arthritis is a chronic, progressive auto-immune systemic disorder. The joints commonly affected are those of the hand and feet. In advanced cases, most of the synovial joints get affected.

Arthritis involves breakdown of cartilage. As there is less cartilage, bones rub together causing pain, swelling and stiffness. Joint shape gets disturbed. Fibrosis can result causing restriction of movement. Granulation tissue spreads to tendons and muscles which weaken and get atrophied.

Pathophysiology The exact cause is not understood. It is thought to be an auto-immune disease which affects the joints and also the heart, blood vessels and skin. Antigen–antibody complexes are formed and seen in the blood and synovial fluid.

Females are more affected and the onset is maximally between 35 and 55 years of age.

Broken bones, wear and tear, and infection predispose one to arthritis.

3. Osteoarthritis

Osteoarthritis is a degenerative disorder affecting one or more joints where there is pain and restriction of movement of the affected joint. There are two types of osteoarthritis—primary and secondary.

Primary osteoarthritis is more common and is related to aging. There is breakdown and degeneration of cartilage. Articular cartilage becomes thinner. Renewal keeps pace with breakdown. Eventually, there is loss of cartilage cushion between the bones. There is friction between the bones and they begin to degenerate. The bone gets inflamed and stimulates new bone outgrowths in the form of a local bony protrusion called **spur**.

Pathophysiology The exact cause is not known. Probably as it is a disorder of the aging process, there could be acceleration of normal aging process due to excessive use.

Osteoarthritis can develop in multiple members of the same family, implying a hereditary–genetic basis for this condition.

Secondary osteoarthritis is secondary to another disease or condition. It could be secondary to trauma, surgery of joint, obesity, gout, diabetes, congenital abnormality of joint and hormonal disorders.

4. Ankylosing Spondylitis

Ankylosing spondylitis is a form of chronic inflammation of the spine affecting the sacroiliac joints and vertebral joints which progressively get ossified. The tendency to develop this condition is probably due to genetic inheritance.

5. Psoriatic Arthritis

Psoriatic arthritis is a chronic disease characterized by inflammation of the joints and the skin, especially the nails. The cause is not known. A combination of genetic and immune and environmental factors are probably involved.

6. Rheumatic Arthritis

Rheumatic fever is an inflammation of the body's organ systems, especially the joints and the heart that can develop as a complication of streptococcal infection of the throat. It involves usually the wrists, elbows, knees and ankles. This kind of arthritis usually resolves without complications.

7. Reiter's Syndrome

Reiter's syndrome is characterized by a triad of arthritis, urethritis and conjunctivitis and by lesions of the skin and

mucus membranes. It usually develops following an intestinal or urinary or genital-tract infection. It is more likely to occur in individuals who have a particular genetic predilection. The infective agent is *Chlamydia trachomatis*. Usually, the joints of the lower limb are affected.

8. Septic Arthritis

Septic arthritis is the purulent invasion of a joint by an infectious agent. Bacteria are carried by the bloodstream from an infectious focus elsewhere, introduced by a skin lesion, that penetrates the joint or extension from adjacent tissue. Most of the time, the joint which gets affected has been damaged by previous injury or arthritis. Microorganisms must reach the synovial membrane of the joint.

9. Gout

Gout is one of the most painful forms of arthritis. It is a chronic and progressive disease. It results from an overload of uric acid in the body which leads to the formation of tiny crystals of urate that deposit in tissues of the body especially in and around the joints causing recurrent joint inflammation. After repeated attacks, permanent damage may occur and there follows deformity and loss of function. The joints usually affected are the metatarsalphalangeal joint of the great toe, the ankle, knee, wrist and elbow joints. Renal calculi and decreased renal function is also seen.

REVIEW QUESTIONS

1. Explain the structure and functions of bone.
2. Describe the types of bones and discuss the structure of the long bone.
3. Describe the events of ossification.
4. Describe development of bone and how bone growth is regulated.
5. Give the names of skull bones. Describe them.
6. Describe cranial cavity with importance to applied anatomy.
7. Explain the characteristics of typical vertebra with a diagram.
8. Classify joints with examples. Describe them.
9. Discuss different types of synovial joints with appropriate examples.
10. What are the different types of joint movements?
11. Describe various joint disorders.
12. Write a note on various types of arthritis.
13. Draw a labeled diagram of ankle bones.
14. Write short notes on:
    a. Thoracic cage
    b. Cartilaginous joints
    c. Rheumatoid arthritis
    d. Blood supply of long bones
    e. Fibrous joints
    f. Synovial joints
    g. Joint movements
    h. Composition of bone
    i. Bone development
    j. Osteoarthritis
    k. Gout
    l. Osteoporosis

Chapter

6 Muscular System

- **CLASSIFICATION**
  - Striated
  - Nonstriated
  - Voluntary
  - Involuntary
  - Skeletal
    - Anatomy
    - Physiology
    - Properties
      - Contractility
      - Staircase phenomenon
      - Fatigue
      - Contracture
      - Muscle heat
    - Metabolism and energy production
    - Effect of exercise on body
      - Muscles, CVS, RS
      - Temperature
    - Muscles of the body
      - Head and face
      - Neck
      - Eyeball
      - Chest
      - Back
      - Abdominal wall
      - Shoulder girdle
      - Upper arm
      - Forearm
      - Hand
      - Hip joint
      - Thigh
      - Leg
      - Foot

- **Smooth**
  - **Electrical activity**
  - **Ionic basis of action potential**
- **Cardiac**
- **Diseases**
  - **Muscular dystrophy**
  - **Inflammatory myopathy**
  - **Polymyositis**
  - **Myopathies**
  - **Myasthenia gravis**
  - **Periodic paralysis**
  - **Myotonia**
  - **Fatigue**
  - **Muscle cramps**
  - **Sprain**
  - **Myalgia**

Introduction

The human body contains more than 650 individual muscles which are attached to the skeleton. The main function of the muscular system is to provide movement for the body. There are three types of muscle tissue—skeletal, smooth and cardiac. They have the ability to contract, which allows body movements and functions. They also have the ability of converting chemical energy and energy stored in nutrients into mechanical energy and energy of movement respectively.

6.1 CLASSIFICATION OF MUSCLES

Muscles can be classified in three different ways:

I According to Presence or Absence of Striations

1 Striated muscle
2 Nonstriated muscle

II. According to Whether They are Under Voluntary Control

1 Voluntary muscle
2 Involuntary muscle

III. According to Function

1 Skeletal muscle
2 Smooth muscle
3 Cardiac muscle

6.1.1 Striated Muscles

In each muscle cell, a large number of transverse lines, called **cross striations**, are seen under a light microscope. These muscles are called skeletal, voluntary or striped muscles (due to the striations). They are under voluntary control.

Some experts also take cardiac muscles to be striated.

6.1.2 Nonstriated Muscles

These muscles do not have cross striations. Under the microscope, the cells appear spindle shaped with a central nucleus. A fine membrane surrounds each fiber. Bundles of fibers form sheets of muscle. They are called nonstriated or involuntary muscles and are not under our conscious control. They are found in the walls of hollow organs, e.g., alimentary tract, ducts of glands, walls of blood vessels, excretory-system organs, etc.

6.1.3 Voluntary Muscles

Voluntary muscles are the skeletal muscles because they are under voluntary control. Microscopically, they are roughly cylindrical in shape. They may be even as long as 35 cm. Each cell is actually called a **fiber**. There are many nuclei. The cell membrane is called **sarcolemma** and the cytoplasm of the muscle fiber is called **sarcoplasm**.

The sarcoplasm contains many mitochondria, myoglobin, bundles of myofibrils and glycogen.

The muscle fibers run parallel to one another and when seen under the microscope, appear as dark and light bands. So they are called striped or striated muscles.

6.1.4 Involuntary Muscles

Cardiac and smooth muscles are involuntary muscles. Their activities cannot be controlled at will.

6.1.5 Skeletal Muscles

Muscle mass comprises the largest single organ of the body. Each muscle consists of single cells or fibers, embedded in a matrix of collagen. The cells are long and slender. They are multinucleated and arranged parallel to one another. They appear cylindrical in shape. The normal length is 1 to 4 cm but could be even as long as 35 cm. The diameter of muscle fibers varies from 10 to 100 microns.

1. Anatomy

Each muscle cell is enclosed by a cell membrane, also known as **plasmalemma** or **sarcolemma**. The cytoplasm is called sarcoplasm. Many structures are embedded in the sarcoplasm. They are nuclei, myofibril, Golgi apparatus, mitochondria, sarcoplasmic reticulum and ribosomes.

The muscle fibers, when viewed under a microscope, show well-marked transverse dark and light bands and so they are also called striated or striped muscle.

These alternating light and dark bands form sections which are also called **segments** or **discs**.

The light band is called the **J band,** and the dark band is called the **Q disc**.

The bands of adjacent myofibrils are placed side by side and this gives the characteristic appearance of cross striations in the muscle fiber. (See Fig. 6.1)

Sarcomere is the structural and functional unit of the skeletal muscle. Each sarcomere extends between two 'Z' lines of myofibril. 'Z' line divide 'J' or 'I' bands into two.

Each myofibril contains many sarcomeres, arranged in series throughout the length of the myofibril.

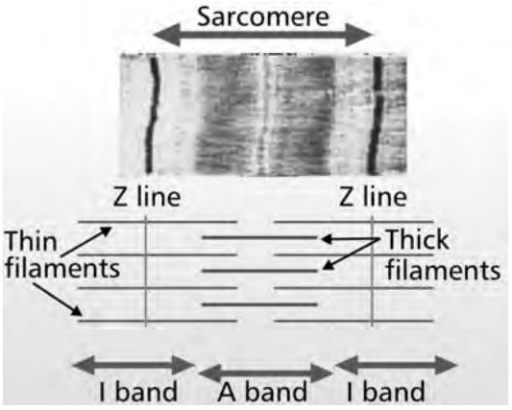


Fig. 6.1 *Striated muscle*

The sarcomere consists of many threadlike protein filaments called **myofilaments**. There are two types of myofilaments and they are the contractile elements of the muscles.

They are

1. Actin filaments
2. Myosin filaments

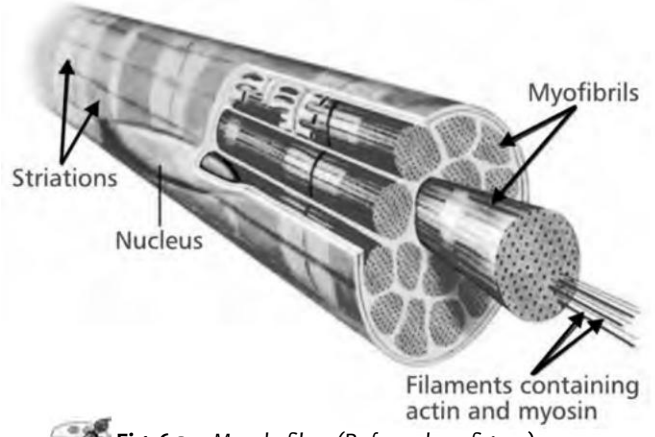


Fig. 6.2 *Muscle fiber (Refer colour figure)*

Actin filaments are thin filaments and extend from either side of the 'Z' line and enter into 'A' band up to 'H' zone. **Myosin filaments** are thick filaments and are situated in 'A' band.

The principal force-generating components are these actin and myosin molecules. These myofilaments are arranged in interdigitating matrices capable of sliding across each other.

The sarcolemma has a unique feature. It has holes in it. These 'holes' lead into tubes called **transverse tubules** or **'T' tubules**. These tubules pass down into the muscle cell and go around the myofibrils. They do not open into the interior of the muscle cell. The function of 'T' tubules is to conduct impulses from the surface of the cell down into the cell and, specifically, to another structure in the cell called the **sarcoplasmic reticulum**.

2. Physiology

Skeletal muscle is voluntary muscle. Contraction requires a nervous impulse. A muscle fiber is excited via a motor nerve that generates an action potential which spreads along the sarcolemma and the transverse tubular system into the deeper parts of the muscle fiber to the sarcoplasmic reticulum. In a relaxed muscle, there is a very high concentration of calcium (Ca) in the sarcoplasmic reticulum and a very low concentration in the sarcoplasm (and, therefore, among the myofibrils and myofilaments). The membrane has special openings, or 'gates', for calcium. These 'gates' are closed and calcium cannot pass through the membrane.

When an impulse travels along the membrane of the sarcoplasmic reticulum, Ca gated channels open and Ca diffuses out of the sarcoplasmic reticulum into the sarcoplasm and comes in contact with the myofilaments. The binding sites in the troponin molecules get filled with Ca, which alters the shape and position of troponin. This leads to movement of the tropomyosin (altered troponin) molecule and permits the myosin head to turn and move towards the actin head. The myosin head gets tightly attached to actin and pulls the actin filament. Many myosin heads are necessary to pull the full thin myofilaments because one myosin head cannot pull the entire thin myofilaments. Cross-bridges develop.

When the swivel is complete, Adenosine Tri Phosphate (ATP) fits into the binding site on the cross-bridge and breaks the cross-bridge between actin and myosin. The myosin head swivels back, ATP breaks to Adenosine Di Phosphate (ADP) and phosphate. The head originally now gets attached to new actin molecules. Again, the myosin head swivels or turns and the cycle continues. So, actually, the myosin and actin filaments slide past one another and this is called the **sliding-filament theory.**

Thus, the thin actin filaments slide past the thick myosin filaments towards the center of 'H' zone and approach the corresponding actin filament from the next 'Z' line. The 'Z' line also approaches the end of the myosin filament. So, the 'H' zone and 'I' bands are shortened. The sarcomere shortens and there is shortening of skeletal muscle. Sarcoplasmic reticulum is now not permeable to Ca and hence, it dose not diffuse out. Ca leaves the troponin molecule and it returns to its original form. Tropomyosin also comes and gets attached to the myosin head, the myosin leaves actin and the muscle relaxes.

The muscle relaxes when the nerve impulse stops. The cross-bridges break, filaments slide apart and the sarcomere returns to its original length.

3. Properties

(a) Contractility Muscles can be excited both by direct stimulation and indirect stimulation through a nerve. When

a skeletal muscle is stimulated, it contracts and the muscle shortens. This contraction is of two types:

- **Isotonic Contraction** In this type of contraction, there is change in the length of the muscle fiber while the tension remains the same. The best example is flexion of the arm due to contraction of biceps and brachialis without any opposing resistance.
- **Isometric Contraction** In this type of contraction, there is increase in tension but length of the muscle remains the same. This is seen when heavy objects are lifted, e.g., against gravity or resistance.

Thus, the physical changes that take place during muscle contraction is a change in the tension developed in the muscle or change in the length of the muscle.

(b) Staircase Phenomenon When stimuli are applied at 2-second intervals, without changing the strength of stimuli for the first few contractions, the force is gradually increased in the successive contractions with increase in amplitude in few contractions and then the force of contraction remains same. This is due to a time interval of 2 seconds between stimuli, which produces beneficial effect, and hence facilitates force of successive contraction.

(c) Fatigue Rapid and repeated stimuli of muscle leads to decrease in excitability and contractility of muscle, a phenomenon called fatigue. This could be due to hypoxia, accumulation of lactic acid and pyruvic acid, depletion of energy and inability to repolarize after depolarization.

Actually, the phenomenon of fatigue is not in the muscle but takes place at the neuro-muscular junction because of depletion of acetylcholine.

(d) Contracture Contracture is a partial contracted state, which is prolonged and reversible and achieved due to repeated stimulation. It is due to fatigue.

Other forms of contracture are tetanic contraction, tonic contraction, rigor mortis and clonus.

- **Tetanic contraction** is a form of sustained contraction due to a combination or summation of many twitches followed rapidly in succession.
- **Tonic contraction** is also a state of tone of the muscle and is a normal phenomenon, whereby muscles remain in a state of partial contraction.
- **Rigor mortis** is the stiffness of the muscle, which occurs after death, and is permanent and irreversible.
- **Clonus** is a state of repeated contraction and summation which results from contraction starting before completion of relaxation.

(e) Muscle Heat Body temperature rises, during and after exercise, by metabolic reactions—aerobic and anaerobic.

During exercise, due to contraction of muscles, heat is liberated in the absence of oxygen. Anaerobic glycogenolysis and glycolysis occurs. Glycogen is converted into glucose1-phosphate which again is converted into lactic acid. The heat produced thus is called **initial heat**.

Once the muscular activity stops, delayed heat is produced. It occurs only in the presence of oxygen. Aerobic chemical changes take place and occur in **Kreb's cycle**.

4. Metabolism and Energy Production

Muscle fibers are of two types—fast twitch and slow twitch. Both are distributed throughout the body.

- **Fast-twitch fibers** store glycogen within the cells of the fiber and is the major source of energy, which is provided in the form of ATP. To utilize this energy, by a process known as **glycogenolysis**, glycogen is converted into glucose and further metabolized to pyruvic acid and lactic acid. This is called **glycolysis**. It takes place in the absence of oxygen, and two ATP molecules are produced for one molecule of glucose metabolized. Lactic acid diffuses into the blood and reaches the liver, where it is again converted into glucose and glycogen through **Cori's cycle**. The glycogen stored here is 1% of the muscle mass which gets quickly depleted during exercise. ATP can be produced for a maximum of 90 seconds. As the ability to produce ATP and energy is limited, these fibers get fatigued quickly.
- **Slow-twitch fibers** require glycogen, which they get through a network of capillaries. The energy production is slower here and is sustained for a longer time. Hence they do not fatigue as quickly as fast-twitch fibers.

Mitochondria also help in energy production by aerobic pathway that involves oxygen and certain respiratory enzymes. Enzymes add phosphate to carbon chains. Hydrogen and carbon bonds are broken. Energy is liberated which is used to synthesize ATP. This process is called **oxidative phosphorylation**. Glucose breaks down and pyruvic acid is liberated. This is converted to coenzyme A, which is metabolized in the citric-acid cycle. Enzymes remove hydrogen and carbon from organic acids and release energy.

5. Effect of Exercise on Body

(a) Muscle and Exercise Whenever exercise is carried out, either in the form of running or swimming or jogging or any other strenuous activity, several things happen in the body. The heart beats faster, muscles ache, the body sweats and breathing becomes faster.

To meet the needs of the working muscle, the body has a response involving the heart, nervous system, lungs, skin and blood vessels.

When the body exercises and the muscles work, they (muscles) start making a demand on the rest of the body. Practically, every system either focuses on helping the muscles to do their work or shut down.

Muscles use ATP for their energy source, for which they need the following:

- They need oxygen, because chemical reactions require ATP and oxygen is consumed to produce ATP.
- They need to eliminate carbon dioxide and lactic acid generated during chemical reactions.
- They have to get rid of heat, as the working muscle generates heat.

Hence, to continue exercising, the muscles must continuously make ATP. The body must supply oxygen to the muscles and eliminate the waste products and heat. The more strenuous the exercise, the greater the demands of working muscles.

If the needs are not met with, the body gets exhausted. It cannot keep going, and then exercise will cease.

(b) CVS and Exercise Exercise causes an increased demand on the CVS, as oxygen demand by the muscles increases. Metabolic processes are speeded and more waste is created. More nutrients are used and the body temperature rises. The cardiovascular system must regulate these changes to meet the increasing demands of the body so that the body can function efficiently.

The cardiovascular system serves the following functions during exercise—it delivers oxygen to the working muscles, transports heat from the muscles to the skin, oxygenates blood by returning it to the lungs, and delivers nutrients to the active tissues.

(c) Respiration and Exercise During exercise, the body burns its supplies faster than it does under normal conditions. The cells operate at a higher level and there is increased use of oxygen and more production of carbon dioxide. The medulla gets stimulated by the increased carbon dioxide and the rate and depth of respiration increases to dispose carbon dioxide and bring in more fresh oxygen.

(d) External Temperature and Exercise Heat, i.e., sunshine, adds a load on the heart. The heart works more to provide blood and oxygen to the exercising muscles. At the same time, blood has to be shunted to the skin where it can be cooled by the evaporation of sweat. For rise of one degree of body temperature, the heart rate increases by 10 beats per minute. Exercise, higher body temperature and the added work of shunting blood, increases the stress on the heart. Hence it is advisable to exercise in the cooler morning or evening hours in order to minimize the thermal stress.

Increase in the temperature around the muscle causes increase in excitability, decrease in viscosity of the muscles and acceleration of chemical processes involved in contraction and relaxation of the muscle.

If the temperature is very high, the muscle undergoes sustained contraction which is irreversible. If temperature is very low, nerve impulse conduction is abolished and hence no contraction takes place.

Muscles of the Body

Striated muscles constitute the principal organ of locomotions. There are more than 600 separate muscles which make up 40% of the body weight. Muscles are attached to bones, cartilages, ligaments and occasionally to skin. Long muscles are seen in the limbs. Broad muscles are found in the trunk, and flat and thin muscles are seen below the skin. Muscles are named depending on their shape, size, position and functions that they perform.

Muscles are joined to bones through a dense band of tissue called the **tendon**. One end is called the origin which is fixed, while the other moveable end is called the insertion.

A single muscle consists of thousands of muscle fibers which lie in the longitudinal axis.

Table 6.1 *Muscles of the Head and Face*

Name	*Situation*	*Action*
Occipito-frontalis		
Occipital	Under the skin, over the occipital bone	Raises the eyebrows
Frontalis	Under the skin, over the frontal bone	Raises the eyebrows
Levator palpebrae superioris	Extends from posterior part of orbital cavity to upper eyelid	Raises the eyelid
Orbicularis oris	Around the mouth and blends with the muscles of the cheek	Closes the lips and shapes the mouth for whistling when contracted strongly
Orbicularis oculi	Surrounds the eye, eyelid and around palpebral fissure	Closes the eyes and on tight closing, screws the eyes
Buccinator	In the cheek	Draws the cheek towards the teeth during chewing and contracts the cheek for expulsion of air from the mouth
Masseter	Extends from zygomatic arch to the angle of the jaw	Helps in chewing and closing of the jaw to exert pressure on the food
Temporalis	Covers the squamous part of temporal bone, passes behind zygomatic arch and is inserted into the corocoid process of the mandible	Raises lower jaw, closes the mouth and helps in chewing
Pterygoid	In the intra-temporal fossa and extends from the sphenoid bone to the mandible	Pulls the lower jaw forward and closes the mouth

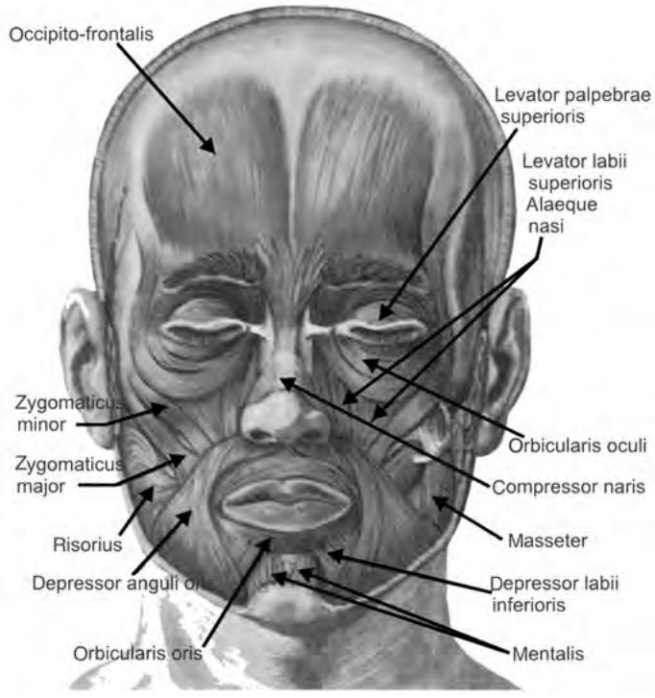


Fig. 6.3 *Muscles of the head and face*

Table 6.2 *Muscles of the neck*

Name	*Situation*	*Action*
Sternocleidomastoid	Arises from manubrium sterni and the clavicle and extends to the mastoid process of the temporal bone	When one muscle contracts it turns the head to that side and when both contract the head is thrown back
Platysma	On the lateral side of neck	Wrinkles the skin of the neck and depresses the jaw
Trapezius	Covers the shoulder and back of neck; upper part is attached to occipital protruberance, medial part to transverse process of cervical and thoracic vertebrae and lateral part to clavicle and spinous and acromian processes of scapula	Elevation of shoulder and movements of scapula controlled when shoulder moves
Hyoid muscles	Arises from inner side of mandible and attached to the body of hyoid bone	Movement of hyoid bone, larynx and jaw
Capitis muscles	Deeper part of neck from transverse processes of first seven cervical vertebrae and longissimus from transverse process of first four thoracic vertebrae to occipital bone and mastoid process of temporal bone	Flexion and extension of the head

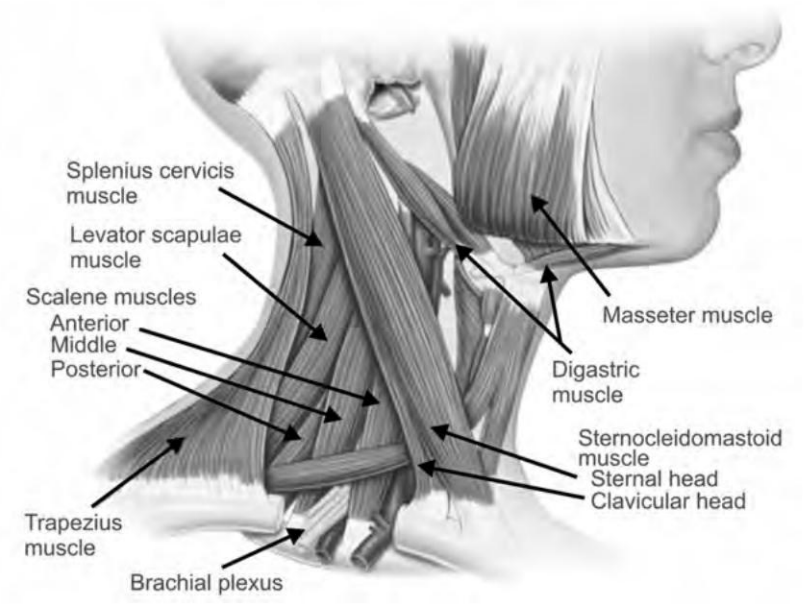


Fig. 6.4 *Muscles of the neck*

Table 6.3 *Muscles of the Eyeball*

Name	*Situation*	*Action*
Superior rectus	Arises from the common tendinous ring attached to orbit around optic foramen and inserted into superior and central part of eyeball	Movement of eyeball superiorly
Inferior rectus	Arises from the common tendinous ring attached to orbit around optic foramen and inserted into inferior and central part of eyeball	Movement of eyeball inferiorly
Medial rectus	Arises from the common tendinous ring attached to orbit around optic foramen and inserted into medial part of eyeball	Adduction of eyeball—medial rotation
Lateral rectus	Arises from the common tendinous ring attached to orbit around optic foramen and inserted into lateral part of eyeball	Abduction of eyeball—lateral rotation
Superior oblique	Arises from sphenoid bone and inserted into superior and lateral part of eyeball	Abduction and depression of eyeball
Inferior oblique	Arises from maxilla in the floor of orbit and inserted between Inferior and lateral part of eyeball	Abduction and elevation of eyeball

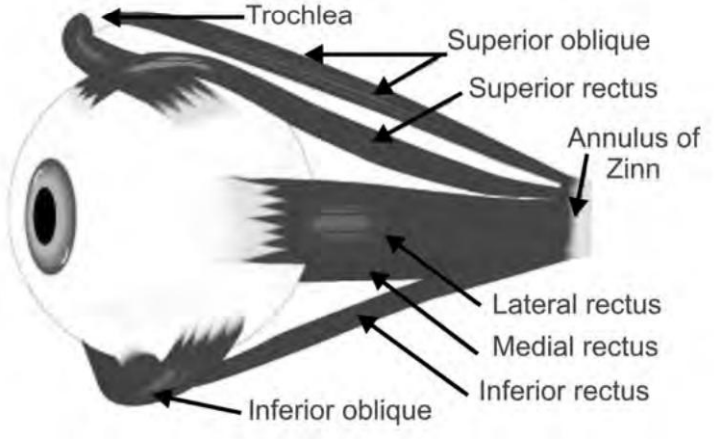


Fig. 6.5 *Muscles of the eyeball*

Table 6.4 *Muscles of the Chest*

Name	*Situation*	*Action*
Pectoralis major	Arises from the sternum and clavicle and insertion is on the humerus; found on the anterior chest wall	Draws the arm forward and towards the body—flexes and adducts
Pectoralis minor	Under pectoralis major muscle and placed between second and fifth ribs and scapula	Draws scapula downward and forward
Serratus anterior	Lateral side of thorax and takes origin from the upper eight ribs	Fixation of scapula, turns the scapula and pulls it downward and forward
Intercostal muscles	Between the ribs	External muscles elevate the ribs and internal muscles depress the ribs
Diaphragm	Between the chest cavity and abdominal cavity; origin is from the sternum, ribs and lumbar vertebrae	Takes part in respiration—when contracts it descends and on relaxation returns to original position

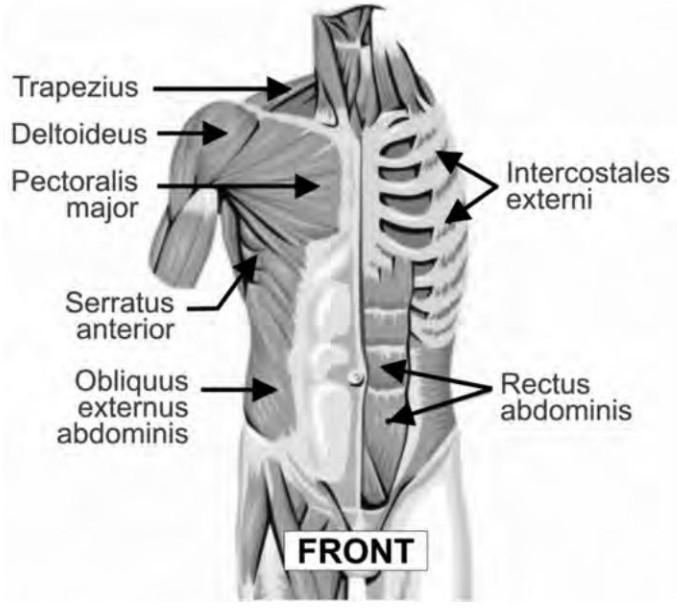


Fig. 6.6 *Muscles of the chest*

Table 6.5 *Muscles of the Back*

Name	*Situation*	*Action*
Teres major	Under rhomboid muscle, originates from inferior angle of scapula and is inserted into the humerus	Extends, adducts and rotates the arm medially
Latissimus dorsi	Arises from posterior part of iliac crest and spinous processes of lumbar and lower thoracic vertebrae and is inserted into the bicipital groove of humerus	Adducts, extends and rotates the arm
Rhomboideus	Upper part of back and under the trapezius, arises from spines of seventh cervical to fifth thoracic vertebrae and inserted into vertebral border of scapula	Draws scapula towards the spine
Sacrospinalis	Side of the vertebral column	Extension of the vertebral column
Quadratus lumborum	Close to the vertebral column extending from iliac crest and ilio lumbar ligament up to 12th rib and first four lumbar vertebrae	Contraction of one muscle causes lateral flexion of lumbar vertebral column and contraction of both muscles causes extension of vertebral column

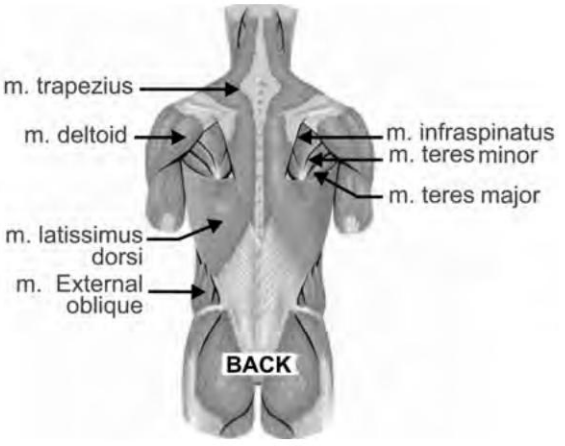


Fig. 6.7 *Muscles of the back*

Table 6.6 *Muscles of the Abdominal Wall*

Name	*Situation*	*Action*
Rectus abdominus	Bilaterally on either side of the median line arising from the transverse part of pubic bone and inserted into the lower ribs and xiphoid process of sternum	Support to the abdomen and abdominal viscera
External oblique	Extends from the lower ribs and inserted into the iliac crest	Both these muscles tense the abdominal wall, support abdominal viscera and flex and rotate the vertebral column
Internal oblique	Below external oblique, fibers at right angles to those of external oblique, arises from iliac crest and spinous processes of lumbar vertebrae and inserted into the lower ribs and linea alba	
Transverses abdominus	Below internal oblique and deepest muscle of the abdominal wall and runs transversely, arises from iliac crest and lumbar vertebrae and inserted into the linea alba	Supports and compresses the abdominal viscera
Psoas	Arises from transverse processes and bodies of lumbar vertebrae, passes across the flat part of ilium and is inserted into the femur	Flexes the hip joint together with iliacus
Quadratus lumborum	Described above	

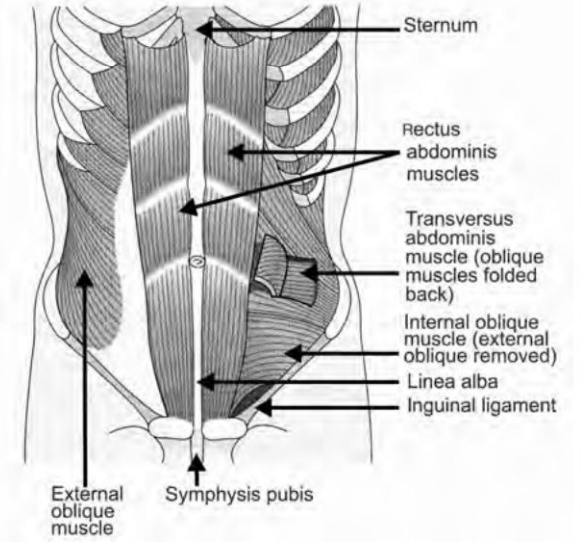
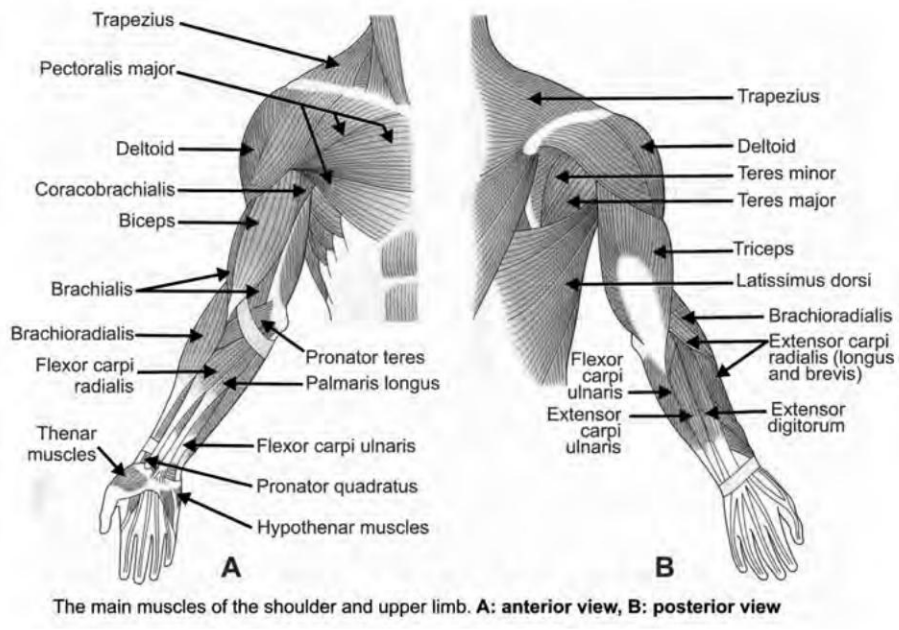


Fig. 6.8 *Muscles of the abdominal wall*

Table 6.7 *Muscles of the Shoulder Girdle*

Name	*Situation*	*Action*
Deltoid—anterior, Middle, posterior	Anteriorly on the upper arm and forms the rounded contour of the shoulder; arises from the clavicle, spine and acromion process of scapula and is inserted into the deltoid tuberosity	Of the shoulder joint Anterior—flexion Middle—abduction Posterior—extend
Supraspinatus	Supraspinous fossa of scapula	Initiation of abduction of arm
Infraspinatus	Infraspinous fossa of scapula	External rotation of flexed arm
Subscapularis	Subscapular fossa of scapula	Rotates the shoulder
Coracobrachialis	Upper aspect of arm, arises from the coracoid process of the scapula, stretches across the shoulder joint and is inserted into the middle third of humerus	Flexes the shoulder joint



The main muscles of the shoulder and upper limb. **A: anterior view, B: posterior view**

Fig. 6.9 *Muscles of the shoulder girdle, upper arm and forearm (flexor muscles)*

Table 6.8 *Muscles of the Upper Arm*

Name	*Situation*	*Action*
Biceps	Anteriorly on the upper arm, short head arises from the coracoid process of the scapula; long head arises from the rim of glenoid cavity; insertion is into the radial tuberosity	Helps to stabilize the shoulder joint and keeps the arm attached to the shoulder, flexion of arm and supination of forearm
Brachialis	Anterior aspect of upper arm deep to the biceps, originates from the shaft of humerus and is inserted into the ulna	Flexes the elbow joint
Triceps	Posterior aspect of upper arm, arises from three heads—one from the scapula and two from posterior surface of humerus and insertion is on the olecranon process of the ulna	Extends the forearm and adducts the arm, also helps to stabilize the shoulder joint
Brachioradialis	Posterior aspect of upper arm in the lower part, arises from the lower part of humerus and inserted superior to styloid process of radius	Flexion of semipronated arm

Table 6.9 *Muscles of the Forearm*

Name	*Situation*	*Action*
Flexor carpi radialis	Anterior surface of forearm, originates from medial epicondyle of humerus and inserted into second and third metacarpal bones	Radial flexion of wrist and with extensor carpi radialis abducts the wrist
Flexor carpi ulnaris	Medial aspect of forearm, originates from medial epicondyle of humerus and inserted into pisiform, hamate and fifth metacarpal bones	Ulnar flexion of wrist and with extensor carpi ulnaris, adducts the wrist
Extensor carpi radialis longus and brevis	Posterior aspect of forearm, originates from lateral epicondyle of humerus and inserted into second and third metacarpal bones	Extend and abduct the wrist
Pronator quadratus	Distal part of forearm, arises from distal part of shaft of ulna and inserted into distal part of shaft of radius	Pronation of forearm
Pronator teres	Obliquely across upper third of front of forearm, arises from medial epicondyle of humerus and coracoid process of ulna and is inserted into the lateral surface of shaft of radius	Pronation of forearm
Supinator	Obliquely across posterior and lateral aspect of forearm, arises from lateral epicondyle of humerus and upper part of ulna inserted into lateral surface of upper third of radius	Supination of forearm
Extensor carpi ulnaris	Posterior surface of forearm, arises from lateral epicondyle of humerus and inserted into fifth metacarpal bone	Extends and adducts the wrist
Extensor digitorum	Posterior surface of forearm, arises from lateral epicondyle of humerus and inserted into middle and distal phalanges of each finger	Extension of proximal phalanges
Abductor pollicis longus	Posterior surface of middle of forearm, arises from posterior surface of middle of radius and ulna and inserted into first metacarpal	Abduction of thumb
Extensor pollicis longus	Posterior surface of middle of forearm, arises from posterior surface of middle of ulna and inserted into base of distal phalanx of thumb	Extension of distal phalanx of thumb
Extensor pollicis brevis	Posterior surface of middle of forearm, arises from posterior surface of middle of radius and inserted into base of proximal phalanx of thumb	Extension of proximal phalanx of thumb
Extensor indicis	Posterior surface of lower part of forearm, arises from posterior surface of ulna and inserted into tendon of extensor digitorum of index finger	Extension of proximal phalanx of index finger
Palmaris longus	Anterior aspect of upper third of upper arm origin from medial epicondyle of humerus and inserted into flexor retinaculum	Weak flexion of wrist joint
Flexor pollicis longus	Anterior aspect of upper third of upper arm, arises from anterior surface of radius and inserted into base of distal phalanx of thumb	Flexion of terminal phalanx of thumb
Flexor digitorum profundus	Anterior aspect of upper third of upper arm on the ulnar side, origin from anterior medial surface of body of ulna and inserted into base of distal phalanx of fingers	Flexion of terminal phalanx of second and third fingers
Flexor digitorum superficialis	Anterior aspect of forearm, arises from medial epicondyle of humerus coronoid process of ulna and lateral margin of anterior surface of radius and inserted into middle phalanx of each finger	Flexion of middle phalanges

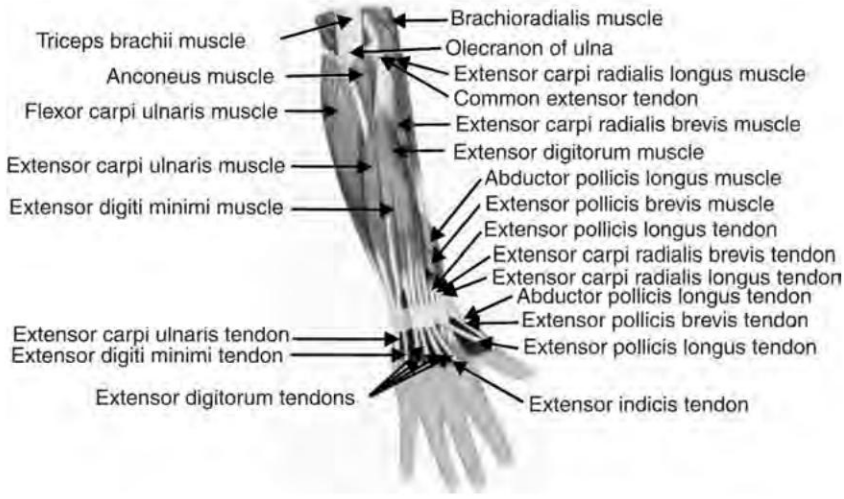


Fig. 6.10 *Posterior muscles of the forearm*

Table 6.10 *Muscles of the Hand*

Name	*Situation*	*Action*
Abductor pollicis brevis	Lateral aspect of palm, arises from flexor retinaculum scaphoid and trapezium and inserted into lateral side of proximal phalanx of thumb	Abduction of thumb at carpometacarpal joint
Opponens pollicis	Lateral aspect of thumb, flexor retinaculum and trapezium and inserted into lateral side of first metacarpal	Opposition of thumb against little finger
Flexor pollicis brevis	Lateral side of proximal phalanx of thumb, flexor retinaculum, capitate trapezoid and trapezium and inserted into lateral side of proximal phalanx of thumb	Flexion of proximal phalanx of thumb
Adductor pollicis	Medial side of proximal phalanx of thumb, arises from capitate and second and third metacarpals and inserted into medial side of proximal phalanx of thumb	Adduction of thumb against second finger
Abductor digiti minimi	Medial side of palm, arises from pisiform and tendon of flexor carpi ulnaris and inserted into medial side of proximal phalanx of little finger	Extension (abduction) and flexion of little finger
Flexor digiti minimi	Medial side of palm, arises from flexor retinaculum and hamate bone and inserted into medial side of proximal phalanx of little finger	Flexion of little finger
Lumbricals	Arise from lateral side of tendons and flexor digitorum profundus of each finger and inserted into lateral side of tendons of extensor digitorum on proximal phalanges of each finger	Flexion of each finger at metacarpophalangeal joints and extension at interphalangeal joints
Palmer interossei	Arise from the sides of shaft of metacarpals of all digits except the middle one and are inserted on the sides of bases of proximal phalanges of all digits except the middle one	Adduction and flexion of each finger at the metacarpophalangeal joints
Dorsal interossei	Arise from the adjacent sides of metacarpals and are inserted into the proximal phalanx of each finger	Abduct and flex fingers 2, 3, 4 at metacarpophalangeal joints and extend each finger at interphalangeal joints

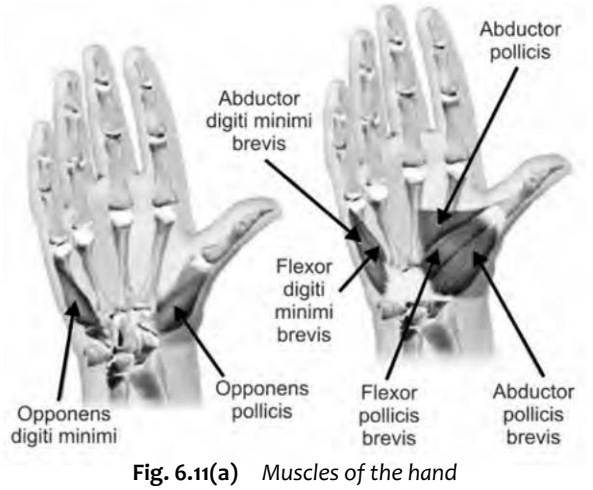


Fig. 6.11(a) *Muscles of the hand*

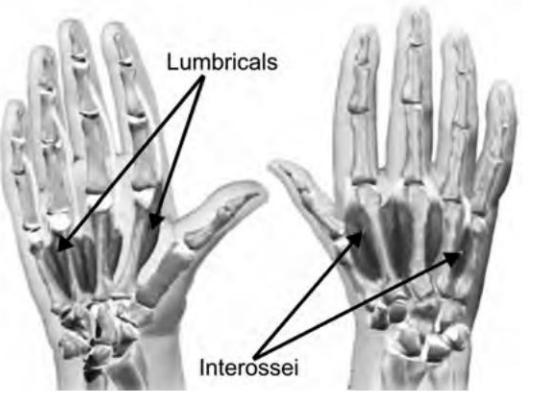


Fig. 6.11(b) *Muscles of the hand*

Table 6.11 *Muscles of the Hip Joint*

Name	*Situation*	*Action*
Ilio psoas	External side of hip, iliacus arises from the iliac crest and psoas from transverse processes and bodies of lumbar vertebrae and both join and are inserted into lesser trochanter of femur	Hip flexion from semiflexed and externally rotated position; flexes trunk on the hip
Adductor longus, magnus and brevis	Inner side of thigh, originate from pubic bone and inserted into linea aspera of femur	Adduction of thigh
Gluteus maximus	Upper, outer part of hip, arises from iliac crest, sacrum and coccyx and inserted into linea aspera of femur	Extension of thigh
Gluteus medius	Outer aspect of hip and upper thigh, arises from ilium and inserted into greater trochanter	Abduction and internal rotation of thigh
Gluteus minimus	Outer aspect of hip and upper thigh, arises from ilium and inserted into greater trochanter	Abduction and internal rotation of thigh
Obturator internus and externus	Inner side of hip and upper thigh, internus arises from inner surface of obturator foramen and externus from outer surface and insertion is on medial surface of greater trochanter	Lateral rotation and abduction of thigh
Pectineus	Anterior, upper part of thigh, arises from superior ramus of pubis and inserted into pectineal line of femur	Flexion and adduction of thigh
Quadratus femoris	Outer side of upper thigh, originates from ischial tuberosity and inserted in the superior part of inter trochanteric crest	Lateral rotation of thigh and stabilization of hip joint

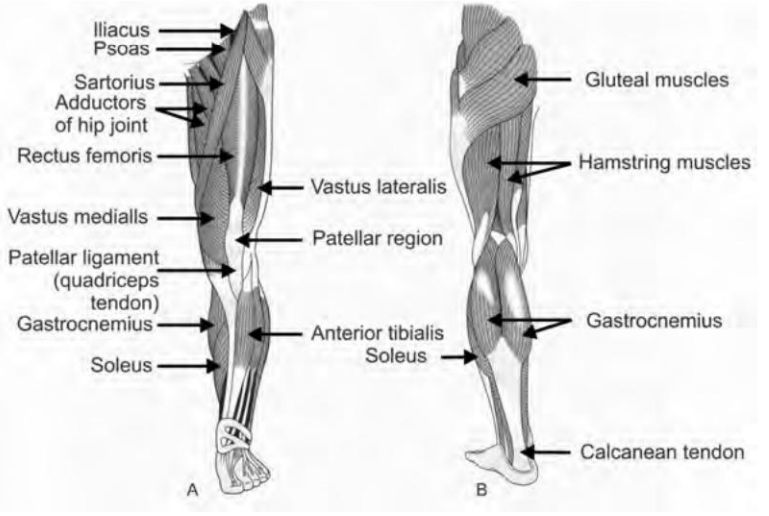


Fig. 6.12 *Muscles of the lower limb*

Table 6.12 *Muscles of the Thigh*

Name	*Situation*	*Action*
Vastus medialis, lateralis and intermedius	Anterior aspect of thigh, arises from upper end of femur and inserted into tibia by patellar tendon	Extension of knee
Rectus femoris	Anterior aspect of thigh, arises from ilium and inserted into tibia by patellar tendon	Extension of knee and flexion of thigh
Sartorius	Anterior aspect of thigh, arises from anterior superior iliac spine and inserted on medial surface of body of tibia	Flexion of knee and abduction and lateral rotation of thigh
Hamstrings—biceps femoris, semimembranosus and semi-tendinosus	Posterior part of thigh, originate from ischium and are inserted into the upper end of tibia	Flexion of the knee and extension of the thigh

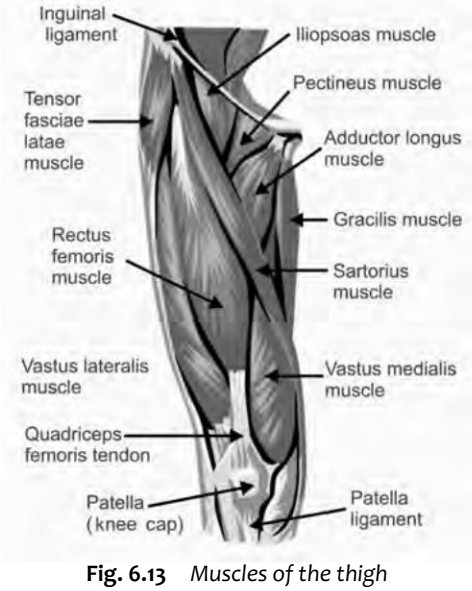


Fig. 6.13 *Muscles of the thigh*

Table 6.13 *Muscles of the Leg*

Name	*Situation*	*Action*
Anterior tibial	Anterior aspect of leg, arises from upper end of tibia and is inserted into the middle cuneiform bone	Dorsiflexion of foot
Extensor digitorum longus	Anterior aspect of leg, arises from lateral condyle of tibia and anterior surface of fibula and is inserted into middle and distal phalanx of toes	Dorsiflexion of toes
Extensor hallucis longus	Anterior aspect of leg, arises from anterior surface of fibula and inserted into distal phalanx of great toe	Dorsiflexion of great toe
Peroneus longus	Anterolateral part of leg, arises from head and body of fibula internal condyle of tibia and inserted into first metatarsal and first cuneiform	Eversion of foot
Peroneus brevis	Anterolateral aspect of leg, arises from body of fibula and inserted into base of fifth metatarsal	Eversion of foot
Peroneus tertius	Anterior aspect of leg, arises from distal third of fibula and inserted into base of fifth metatarsal	Eversion of foot
Gastrocnemius	Posterior and superficial part of leg, arises by two heads, one from each condyle of femur and inserted into calcaneus	Planter flexion of foot
Soleus	Posterior and superficial part of leg, arises from head of fibula and medial border of tibia and inserted into calcaneus	Planter flexion of foot
Tibialis posterior	Posterior and deep part of leg, arises from tibia and fibula and inserted into second, third and fourth metatarsals, navicular and cuboid	Planter flexion and inversion of foot
Flexor digitorum longus	Posterior and deep part of leg, arises from posterior surface of tibia and inserted into distal phalanges of toes	Planter flexion of foot and flexion of toes
Flexor hallucis longus	Posterior and lower part of leg, arises from inferior two thirds of fibula and inserted into distal phalanx of great toe	Planter flexion of foot and flexion of great toe

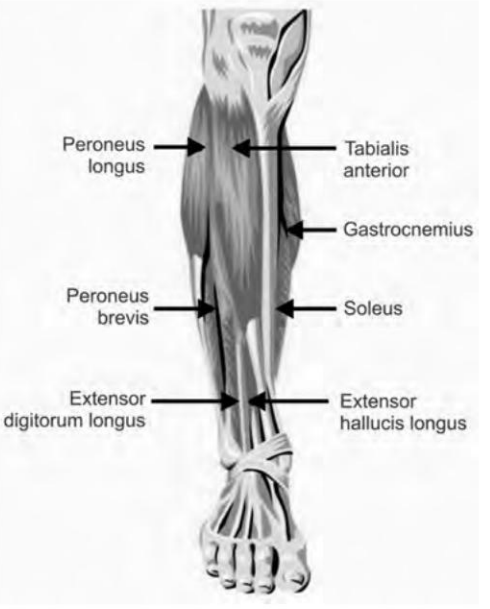


Fig. 6.14 *Muscles of the leg*

Table 6.14 *Muscles of the Foot*

Name	*Situation*	*Action*
Extensor digitorum brevis	Dorsal part of foot, arises from calcaneus and inserted into proximal phalanx of great toe	Extension of toes
Abductor hallucis	Planter and medial side of foot, arises from calcaneus and inserted into medial side of proximal phalanx of great toe	Abduction and flexion of great toe
Abductor digiti minimi	Planter and lateral part of foot, arises from calcaneus and inserted into lateral side of proximal phalanx of little toe	Abduction and flexion of little toe
Flexor digitorum brevis	Planter and central part of foot, arises from calcaneus and inserted into sides of middle phalanx of toes	Flexion of toes
Lumbricals	Planter part of foot, arise from tendons of flexor digitorum longus and inserted into tendons of flexor digitorum longus on proximal phalanges of toes	Extension of toes at interphalangeal joint and flexion of toes at metatarsophalangeal joint
Adductor hallucis	Planter and lateral side of foot, arises from metatarsals two to four and inserted into proximal phalanx of great toe	Adduction and flexion of great toe
Flexor hallucis brevis	Planter part of foot, arises from cuboid and third cuneiform and inserted into medial and lateral sides of proximal phalanx of great toe	Flexion of great toe
Flexor digiti minimi brevis	Planter and lateral side of foot, arises from 5th metatarsal and inserted into lateral side of proximal phalanx of little toe	Flexion of little toe
Dorsal interossei	Dorsal side of foot, arises from adjacent side of metatarsals and inserted into both sides of proximal phalanx of 2nd toe and lateral sides of 3rd and 4th toes	Abduction and flexion of toes
Planter interossei	Planter part of foot, arises from 3rd to 5th metatarsals and inserted into medial side of proximal phalanges of 3rd to 5th toes	Adduction and flexion of toes

(Most of the muscles have been shown in the figures.)

6.1.6 Smooth Muscles

Smooth muscle is responsible for the contractility of hollow organs, such as blood vessels, the gastrointestinal tract, the bladder or the uterus. Its structure differs greatly from that of skeletal muscle.

The most striking feature of smooth muscle is the lack of visible cross striations and hence it is named nonstriated muscle. Smooth-muscle fibers are much smaller (2–5 microns in diameter) than skeletal muscle fibers (10–100 microns).

Smooth-muscle fibers are fusiform or elongated with a centrally situated single nucleus. There are two or more nucleoli. The diameter of the muscle fiber is 2 to 5 microns and its length is 50 to 200 microns.

Smooth muscle is classified as single-unit and multi-unit smooth muscle.

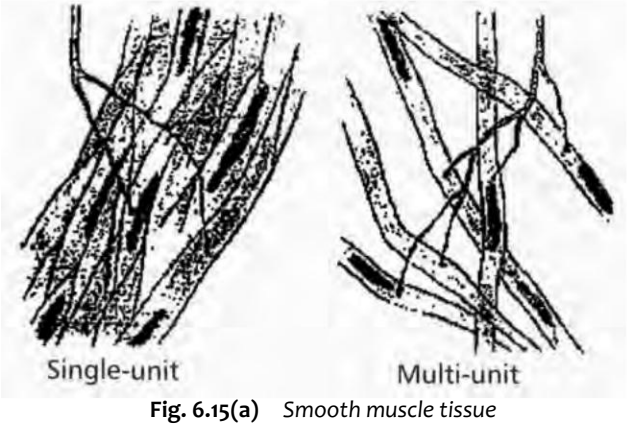


Fig. 6.15(a) *Smooth muscle tissue*

The fibers are assembled in different ways. The muscle fibers making up the **single-unit muscle** are gathered into dense sheets or bands. The fibers run more or less parallel to each other but they are densely and irregularly packed together, so that the narrower portion of one fiber lies against the wider portion of its neighbor.

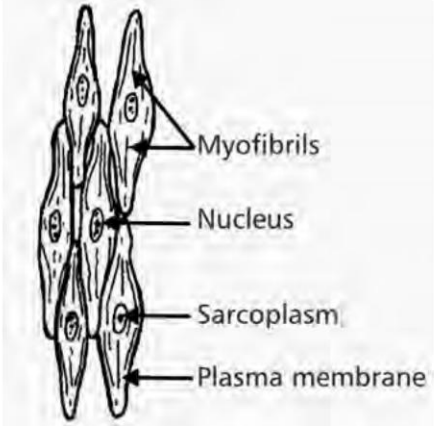


Fig. 6.15(b) *Smooth muscle tissue*

These fibers have connections. The plasma membranes of two neighboring fibers form gap junctions that act as low-resistance pathways for the rapid spread of electrical signals throughout the tissue. Cell-to-cell transmission via communicating gap junctions may be very important in smooth muscles, as in the heart.

The **multi-unit smooth-muscle fibers** have no interconnecting bridges. They are mingled with connective-tissue fibers.

The fibers contract as a whole unit. The fibers of multi-unit smooth muscle are innervated by sympathetic and parasympathetic nerve fibers and respond independently from each other on nerve stimulation.

The muscle fiber contains actin, myosin and tropomyosin components. Troponin is absent from smooth muscles, and their actin regulatory system differs considerably from the thin-filament regulatory system, found in striated muscles. Also, sarcoplasmic reticulum is poorly developed in smooth muscles. **Caldesmon** is a smooth muscle protein that binds reversibly to the actin. It then binds with calcium and calmodulin to form a caldesmon–calcium–calmodulin complex. This combination leads to initiation of contraction. This then dissociates from actin. In contrast to this, **troponin** is a permanent feature of striated muscle and never dissociates from the actin.

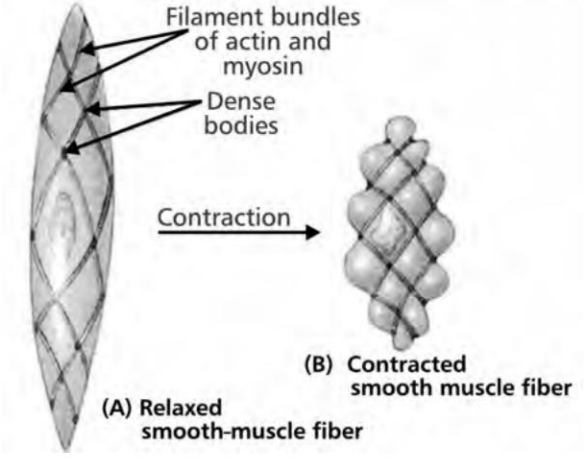


Fig. 6.16 *Smooth-muscle fiber*

Some dense bodies are seen attached to the cell membrane and scattered all over the body of the fibers. Actin filaments are attached to these dense bodies. These dense bodies thus function as Z-lines. Between thick actin filaments, thin myosin filaments are present. The ratio of thin to thick filaments is much higher in smooth muscle than in skeletal muscle. There are cross-bridges between these actin and myosin filaments and this helps in the sliding mechanism.

Smooth muscle thus has only about half the myosin found in striated muscles and lacks their sarcomere organization (actin: myosin = 7:1 in striated muscle, 15:1 in smooth muscle). Smooth-muscle contraction speed is very slow when compared

with voluntary muscle, but it can achieve a much greater degree of shortening.

Electrical Activity in Smooth Muscle

The electrical activity in single-unit and multi-unit smooth muscles are not the same. The electrical activity in multi-unit smooth muscle follows nervous stimuli. Neurotransmitters like acetylcholine and noradrenaline secreted by nerve endings are responsible for electrical changes, leading to contraction. A slight depolarization occurs, which propagates along the entire fiber and there is contraction.

In visceral smooth muscle, an action potential is generated which are of the following types:

- **Spike potential due to nervous stimuli**—It is same as in skeletal muscle except that the amplitude is low.
- **Spike potential initiated by slow wave rhythm—**This rhythm is self-excitatory and leads to rhythmic contraction and contract without external stimuli. Hence they are also called **pacemaker waves**. They are mainly seen in organs like intestines.
- **Action potential with plateau—**This type of action potential is the same as seen in skeletal muscle except that the muscle remains in a depolarized state for a long time.

This type of action potential is responsible for sustained contraction of smooth-muscle fibers. After long depolarized state, slow repolarization occurs.

Ionic Basis of Action Potential

The important difference between the action potential of skeletal and smooth muscle lies in the ionic basis of depolarization.

In skeletal muscle, the depolarization is due to opening of sodium channels and entry of sodium ions into the muscle fiber.

In smooth muscle, it is due to entry of calcium ions rather than sodium ions. Unlike rapid sodium channels, potassium channels open and close slowly. This is responsible for the prolonged action potential in smooth muscles. Calcium ions also play an important role during the contraction of the muscle.

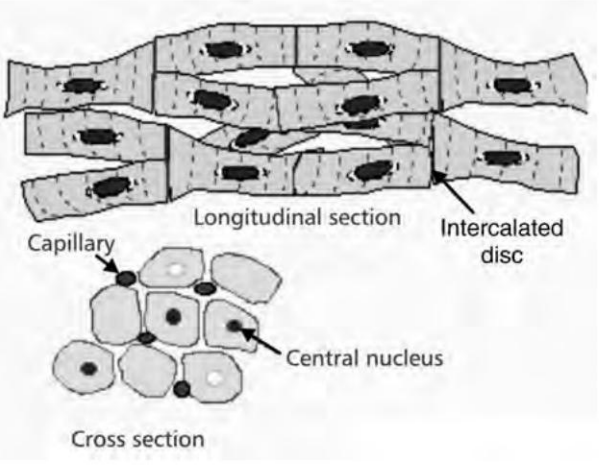


Fig. 6.17 *Cardiac muscles*

Tonic contraction is seen in some visceral organs where they maintain a state of partial contraction called tonus or tone. This is due to tonic contraction without any action potential.

6.1.7 Cardiac Muscles

Cardiac-muscle tissue is exclusively found in the walls of the heart. It is not under voluntary control. When seen under a microscope, cross striations are seen and hence they are also included in striated muscle. They have sympathetic and parasympathetic nerve supply. Each cell is also called a fiber, which is surrounded by sarcolemma. It has one nucleus. Fibers are long and cylindrical but are branched. The end of one cell or fiber is in close contact with the end of the adjacent cell. Thus, forms a three-dimensional network. The place of joining is called a **joint** or **intercalated disc**.

The discs are arranged in such a way that it gives the cardiac muscle the appearance of a sheet of muscle. This arrangement is also helpful in the transmission of a wave of contraction. A wave of contraction spreads from cell to cell across the intercalated discs. So each cell need not be stimulated individually.

Table 6.15 *Difference between Skeletal, Smooth and Cardiac Muscles*

Properties	*Skeletal*	*Smooth*	*Cardiac*
Type	Voluntary	Involuntary	Involuntary
Myofibrils	Striated	Nonstriated	Striated
Location	Attached to bone	Found in walls of visceral organs	Found exclusively in the walls of the heart
Cell type	Long cylindrical fibers	Spindle-shaped	Short cylindrical fibers
Nucleus	Many	One	None
Cytoplasm	Sarcoplasm limited	Sarcoplasm limited	Large amount of sarcoplasm
Size of muscle fiber	Bigger	Smaller	Smaller
Control	Under control of somatic nervous system	Under control of autonomic nervous system	Under control of autonomic nervous system

(*Contd*)

(*Contd*)

Protein content	More	Less	None
Protein	Troponin	Caldesmon and calmodulin	Less
Sarcoplasmic reticulum	Well developed	Poorly developed	
All-or-none law	True for single fiber	True for single fiber	True for whole heart
Refractive period	Short and present during latent period	Longer than skeletal muscle	Present throughout contraction and relaxation
Rhythmicity and automaticity	Absent	Minimally present	They are present independent of nerve activity
Type of contraction	Voluntary, vigorous and fibers contract independently	Involuntary, rhythmic and fibers contract in coordination	Involuntary, often rhythmic and fibers contract in coordination
Fatigue	Get fatigued quickly	Never get fatigued	Difficult to demonstrate

6.1.8 Diseases of Muscles

Diseases of muscles could result from direct abnormalities of the muscles or they could be associated with other general conditions. Muscle diseases can cause weakness, pain or even paralysis. Some known causes include genetics such as muscular dystrophy, inflammation such as myositis, cramps, certain medicines, metabolic causes, and injuries such as sprains. Sometimes there may not even be any cause.

1. Muscular Dystrophy

Muscular dystrophies are a group of progressive, hereditary degenerative diseases of skeletal muscles. There is progressive muscular atrophy (thinning) and weakness. The muscles of the limb girdles (shoulder and pelvic) are involved.

The most frequent types are pseudo-hypertrophic form of Duchenne, and Becker's muscular dystrophy (limb-girdle type and facio-scapular-humeral type).

Other forms are ocular type, dystrophia myotonica and congenital dystrophy.

Duchenne's is the most severe variety and occurs in young children.

There is increased difficulty in walking, running or climbing stairs. The child exhibits a waddling gait and enlargement (hypertrophy) of calf muscles. On getting up, he has to climb on himself and has to put his hands on his knees for support and push himself up.

Pathophysiology There is an abnormal gene and gene product. *Dystrophin* is the protein product of the affected gene, which is the probable cause for dystrophy.

Usually it runs in the family and occurs predominantly in males with females by and large being carriers.

2. Inflammatory Myopathy

Bacterial myositis, an inflammation of muscle tissue, is seen after an injury and is usually localized. Inclusion body myositis is a more severe condition where the person is progressively disabled and succumbs to respiratory infection.

Pathophysiology Usually *Staphylococcus* and *Streptococcus* organisms are responsible for muscle inflammation. In inclusion body myositis, intra-nuclear and intra-cytoplasmic inclusions are seen. The inclusions are suggested to be of viral origin but a virus has not been located.

3. Polymyositis

Polymyositis is a sub-acute, inflammatory, symmetrical weakness of the proximal limb and trunk muscles. Usually all the muscles of the trunk, shoulders, upper arm, hips and thigh are involved. There is also muscle pain along with tenderness. There is difficulty in walking, climbing stairs, standing up from a sitting position and raising the hands above the head.

Pathophysiology The cause is unknown. All attempts to isolate an infective agent have been unsuccessful. Probably an auto-immune mechanism is involved due to its association with a number of other auto-immune diseases.

4. Myopathies

Myopathies are diseases that affect the proximal muscles such as the biceps and deltoid in the upper arm and the quadriceps in the thigh. Myopathies can be caused by inherited defects, by endocrine disorders, by metabolic disorders or by toxins.

All types of myopathies produce weakness and atrophy of skeletal muscles, especially the proximal muscles; distal muscles are less affected. There is difficulty in walking, frequent falls, difficulty in getting up from sitting position and difficulty in climbing stairs.

Congenital myopathies are mitochondrial myopathy, central core myopathy and nemaline myopathy. The inheritance could be autosomal dominant or recessive.

Myopathies of endocrine origin are seen in thyroid dysfunctions like myxedema or thyrotoxicosis; adrenal dysfunction like Cushing disease; pituitary dysfunction; parathyroid dysfunction; diabetes mellitus myopathy and steroid myopathy which is the most common of all.

Toxic Myopathies can be caused by many drugs and toxins. Cholesterol lowering agents, especially statins, can cause

toxic myopathy. Mitochondrial toxins, antimicrotubule drugs, foods, corticosteroids, chloroquine, vincristine, bupivacaine, etc., cause toxic myopathy. There is pain and weakness. If the drug is withdrawn in time, symptoms decrease and patients recover rapidly.

Pathophysiology Intramuscular injection of bupivacaine damages the muscle fibers by disrupting the membrane and allows calcium to enter and destroy the cell. Chloroquine and vincristine disrupt the internal biochemistry of the muscle fiber. Corticosteroids affect the muscle metabolism.

Metabolic myopathies These are a group of hereditary muscle disorders caused by specific enzymatic defects due to defective genes. They are considered primary inborn errors of metabolism. The enzymatic defects affect the ability of the muscle fibers to maintain adequate energy and ATP concentrations and so there is abnormality in muscle energy metabolism. There could be abnormalities of glycogen, lipid, purine or mitochondrial biochemistry.

6. Myasthenia Gravis

Myasthenia gravis is an acquired auto-immune disorder. There is failure of transmission of impulse from the nerve to the muscles. There is a tendency for the muscles to be easily fatigued. Muscular weakness is more after physical exertion particularly of the face, limbs and neck. There maybe drooping of eyelids with diplopia especially in ocular myasthenia. There is difficulty in swallowing and breathing. Weakness recovers partially after rest.

Pathophysiology Autoimmune antibodies destroy the acetylcholine receptors of the neuromuscular junction. Thymus is probably thought to be responsible in some way though the exact mechanism is not known.

7. Periodic Paralysis

Persons with periodic paralysis suffer from recurrent attacks of muscle paralysis which may last from few minutes to 24 hours. Muscles of the legs are more affected and of the arms and trunk to a lesser extent. It is usually seen when the person is resting after vigorous exercise. During the attack the muscles are tender.

8. Myotonia

Myotonia is an uncommon hereditary disease. There is tonic spasm of the muscle after forceful muscle contraction. The spasm is painless. Frequent falls on walking and running is seen. Strong closure of the eyes causes spasm and prevents the eyes from opening quickly. The cause is genetic and could be autosomal dominant or autosomal recessive.

9. Fatigue

Fatigue is a failure of the muscle to sustain force in a prolonged contraction or to reattain force in repeated contractions. It occurs on prolonged use of the muscles as in walking or standing for a long period.

10. Muscle Cramps

A muscle cramp is an involuntarily and forcibly contracted muscle that does not relax. When we move the limbs, the muscles of arms and legs alternately contract and relax. The muscles of head, neck and trunk contract in a synchronized manner to maintain posture. But, a muscle that involuntarily contracts is in a spasm and if the spasm is forceful and sustained, it becomes a cramp. The affected muscle is palpable and visible.

11. Sprain

Sprain is actually affection of ligaments rather than muscles. Ligaments are tough, elastic-like bands that connect bone to bone and stabilize the joints. Due to excessive stretching, the ligament gets injured and there is pain. Ankle and knee sprains are the most common.

A muscular tear in the same manner is called strain. Muscles stretch on movement but, if the stretch is too far, or if stretched while contracting, an injury called a strain will result.

12. Myalgia

Generalized muscle pain is associated with many other conditions like viral infections, malaria, rheumatic fever, typhoid etc. There is associated malaise and weakness. Nothing is known about the pathogenic basis of the muscular pains and remains obscure. Only some facts are noted. Muscle pain is associated with tenderness on exposure to cold, minor trauma. Local heat and massage gives relief.

REVIEW QUESTIONS

1. Classify the muscular system. Describe the structure of cardiac muscle.
2. Describe the structure of skeletal muscle. Discuss the physiology of skeletal muscle contraction.
3. Describe the structure of smooth muscle. Describe the physiology of smooth-muscle contraction.
4. Differentiate between skeletal, smooth and cardiac muscle.
5. Explain properties of cardiac muscle (see CVS).
6. Describe the structure of sarcomere in detail.
7. Describe the properties of skeletal muscle.
8. Explain the effect of exercise on the body at different levels.
9. Write short notes on:
    a. Muscle metabolism
    b. Physiology of impulse transmission
    c. Ionic basis of impulse transmission

Chapter

7 Cardiovascular System

- **ANATOMY**
  - **External features**
    - Apex,
    - Base,
    - Surfaces of heart (anterior, inferior, left),
    - Borders
      - Right atrium
      - Right ventricle
      - Left atrium
      - Left ventricle
  - **Structure of the heart**
    - Pericardium
      - Layers (fibrous, serous)
      - Contents
      - Arterial supply
      - Venous drainage
      - Nerve supply
    - Myocardium
    - Endocardium
  - **Interior of the heart**
    - Heart valves
    - AV valves
    - Semilunar valves
    - Applied anatomy
  - **Blood vessels**
    - Arteries and arterioles
    - Capillaries and sinusoids
    - Anastomosis and end arteries
    - Arterial system
    - Veins and venules
    - Venous system
    - Difference between arteries and veins

- **PHYSIOLOGY**
  - Conducting system
    - SA node
    - AV node
    - Bundle of His
  - Properties
    - Excitability
    - Rhythmicity
    - Conductivity
    - Contractility
  - Cardiac cycle
    - Phases of cardiac cycle
- **HEART SOUNDS**
  - Methods of studying
  - Applied physiology
- **PULSE**
  - Arterial pulse
    - Pulse waves
    - Pulse variants
      - Regularly irregular pulse
      - Irregularly irregular pulse
      - Bounding pulse
      - Pulsus paradoxus
  - Venous pulse
- **FACTORS AFFECTING HEART RATE**
- **ELECTROCARDIOGRAM**
- **CARDIAC ARRHYTHMIAS**
  - Normal electrical activity
  - Tachyarrhythmia
    - Automaticity
    - Re-entry
    - Fibrillation
  - Bradyarrhythmia
    - Symptoms
    - Diagnosis
  - Classification
    - Atrial
    - Junctional
    - Ventricular
    - Atrio-ventricular
    - Ventricular
    - Heart blocks
- **CARDIAC OUTPUT**
  - Maintenance of CO
    - Control of heart rate
    - Control of stroke volume
      - End-diastolic volume
      - Increased sympathetic activity

- Minute volume
- Cardiac index

- Measurement of CO
- Variations in CO
  - Physiological
  - Pathological
- Distribution of CO
- Factors maintaining CO
  - Venous return
    - Muscle contraction
    - Decreased venus compliance
    - Respiratory activity or respiratory pump
    - Vena cava compression
    - gravity
  - Peripheral resistance
  - Blood volume
  - Heart rate

• BLOOD PRESSURE

- Types of Blood pressure
  - Systolic
  - Diastolic
  - Pulse
  - Mean arterial
- Control of Blood pressure
  - Short-term control
    - Baroreceptors
    - Chemoreceptors
    - Higher centers in the brain
  - Long term control
    - Regulation of EFV
  - Hormonal regulation
    - Renin-angiotensin mechanism
  - Local control
- Measurement of BP
- Variations in BP
  - Physiological
  - Pathological

• CIRCULATION

- Arterial circulation
- Venous circulation
- Capillary circulation
- Pulmonary circulation

- Circulation through special regions
  - Coronary circulation
- CBF and its measurement

• VENOUS DRAINAGE—HEART

- ○ Applied Physiology
- ○ Types of Circulation ..... Lymphatic circulation

• INVESTIGATIONS IN CARDIOLOGY

- ○ ECG, Holter monitoring, TMT
- ○ Noninvasive cardiac imaging ..... ECHO cardiography
  - ..... TEE
  - ..... Stress echocardiography
  - ..... Doppler echocardiography
  - ..... Color-flow doppler study
- ○ Nuclear cardiology ..... Basic principles ..... SPECT, PET
  - ..... MRI
  - ..... CT imaging
  - ..... Contrast enhanced CT angiography
- ○ Invasive cardiac procedures ..... Cardiac catheterization
  - ..... Angioplasty
  - ..... CABG surgery
  - ..... Beating heart surgery
- ○ Cardiac disorders ..... Atherosclerosis
  - ..... Coronary heart disease
  - ..... Angina
  - ..... Myocardial infarction
  - ..... Heart failure ..... Right sided
    - ..... Left sided
  - ..... Congenital Heart Disease
  - ..... Vascular disorders
  - ..... Thrombosis
  - ..... Embolism
  - ..... Varicose veins
  - ..... Hypertension ..... Essential hypertension
    - Benign
    - Malignant
    - ..... Secondary hypertension
  - ..... Hypotension

Introduction

The heart, which lies obliquely in the thoracic cavity, is a muscular cone-shaped hollow organ about the size of a clenched fist of the same person. It is located in the middle mediastinum, a little more to the left and is about 10 cm long. The apex lies 9 cm to the left of the midline at the level of 5th intercostal space. The base is at the level of the second rib. The weight of the heart is 225 g in women and slightly heavier in men. The heart is enclosed in a pericardial sac.

The main function of the heart is to pump blood to the various organs of the body.

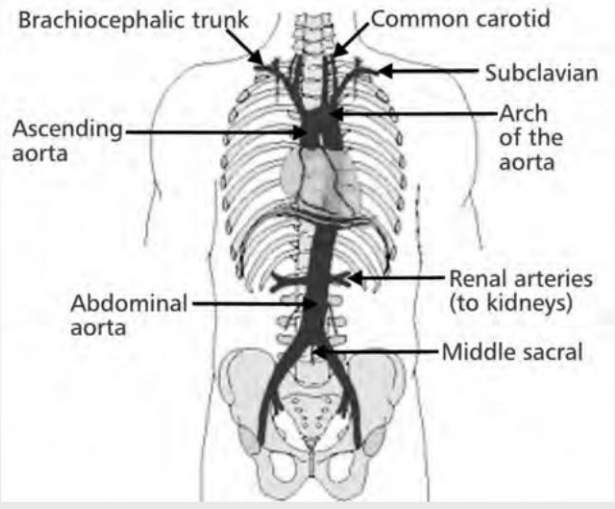


Fig. 7.1 *The heart with its major arteries*

7.1 ANATOMY

7.1.1 External Features of the Heart

The heart is divided into right and left sections by a septum. Each of these (right and left) sections is again divided into upper and lower compartments known as atria and ventricles.

The heart thus has four chambers, two **atria** and two **ventricles**. The upper two chambers are called atria, and the lower two chambers are called ventricles. On the surface, atria are separated from the ventricles by an atrioventricular groove. Atria are separated from each other by the inter-atrial groove and the ventricles are separated from one another by interventricular groove.

The upper part of each atrium has an appendage called the **auricle**.

The heart has an apex, a base, and three surfaces. The surfaces are demarcated by upper, lower, right and left borders.

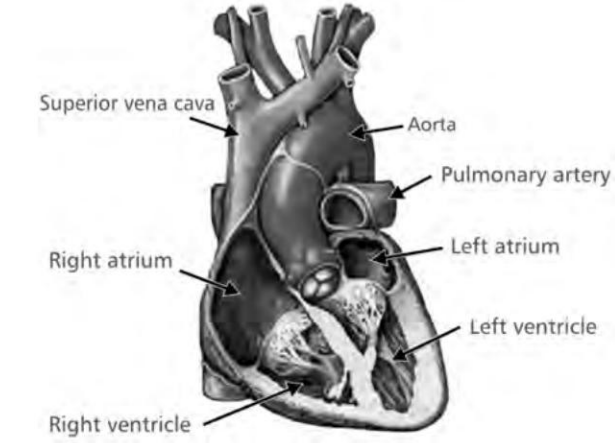


Fig. 7.2 *The heart and its chambers (Refer colour figure)*

1. Apex

The apex is formed by the left ventricle and is directed downwards, forwards and to the left and is overlapped by the anterior border of the left lung. In a thin person, the apex may be seen or felt in the left 5th intercostal space about 9 cm away from the midline.

2. Base

The base of the heart forms the posterior surface. It is formed by the left atrium and by a small part of the right atrium.

3. Surfaces of the Heart

The **anterior surface** is also called the **sternocostal surface**. It is mainly formed by the right atrium and right ventricle and partly by the left ventricle and left auricle. Most of this surface is covered by the lungs but the part behind the cardiac notch of the left lung is uncovered.

The **inferior surface** or the diaphragmatic surface rests on the central tendon of the diaphragm. The right 1/3rd is formed by the right ventricle, and the left 2/3rd by the left ventricle.

The **left surface** is mostly formed by the left ventricle and a small part at the upper end by the left auricle.

4. Borders of the Heart

- The **upper border** is slightly oblique and is formed by the two atria.
- The **right border** is vertical and formed by the right atrium.
- The **inferior border** is nearly horizontal and mainly formed by the right ventricle.
- The **left border** is curved and oblique and mainly formed by the left ventricle and partly by the left auricle.

(a) Right Atrium It is elongated vertically and receives venous blood from the whole body through the superior

and inferior vena cavae and pumps it into the right ventricle through the right atrioventricular opening which is also called the **tricuspid opening**.

It forms the right border of the heart and part of the upper border, the sternocostal surface and the base of the heart.

The upper end is prolonged to form the right auricle.

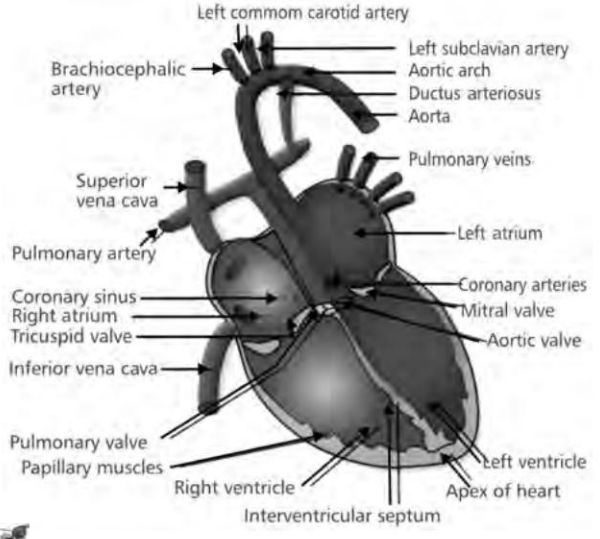


Fig. 7.3 *Structure of a normal heart (Refer colour figure)*

(b) Right Ventricle It is a triangular chamber which receives blood from the right atrium through the tricuspid opening and pumps it to the lungs through the pulmonary trunk and pulmonary arteries.

It forms the inferior border, a large part of the sternocostal surface, and a small part of the diaphragmatic surface of the heart.

(c) Left Atrium It is a quadrangular chamber situated posteriorly. Its appendage, the auricle, projects anteriorly to overlap the infundibulum of the right ventricle.

It forms 2/3rd of the base of the heart.

It receives oxygenated blood from the lungs through four pulmonary veins and pumps it to the left ventricle through the left atrioventricular opening, also called the **mitral valve** or **bicuspid valve**.

(d) Left Ventricle It receives oxygenated blood from the left atrium through the mitral valve and pumps it into the aorta.

It forms the apex of the heart and a part of the sternocostal surface, most of the left border and left surface and left 2/3rd of diaphragmatic surface.

7.1.2 Structure of the Heart

Three layers of tissue form the heart wall.

- Outer layer or pericardium
- Middle layer or myocardium
- Inner layer or endocardium

1. Pericardium

It is a thin outer layer which gives the surface of the heart a smooth, slippery texture. It is a fibro-serous sac, which encloses the heart and the roots of the great vessels. There are two layers to the pericardial sac—the fibrous pericardium and the serous pericardium.

(a) Fibrous Pericardium The fibrous pericardium is the outermost layer of the pericardium. It is a dense connective tissue, protecting the heart, anchoring it to the surrounding walls, and preventing it from overfilling with blood because of its inelastic and fibrous nature.

It is continuous with the outer adventitial layer of the neighboring great blood vessels above and with the pretracheal fascia. It is adherent inseparably to the diaphragm below.

(b) Serous Pericardium The serous pericardium is thin and double-layered, lined by mesothelium. The serous pericardium is further divided into two layers, the **parietal pericardium**, which is fused to and inseparable from the fibrous pericardium; and the **visceral pericardium**, which is a part of the epicardium. The epicardium is the layer immediately outside the heart muscle proper (the myocardium).

In between the parietal and visceral pericardial layers, there is a potential space called the **pericardial cavity**. It is lined by flattened epithelial cells which secretes a fluid into the space. This small amount of fluid allows smooth movement between the two layers when the heart beats.

(c) Contents of the Pericardium

- Heart with cardiac vessels and nerves
- Ascending aorta
- Pulmonary trunk
- Lower half of superior vena cava
- Terminal part of inferior vena cava
- Terminal parts of pulmonary veins

(d) Arterial Supply Arterial supply to the pericardium is from internal thoracic artery, musculophrenic artery and descending thoracic aorta.

(e) Venous Drainage Veins drain into the azygos veins and internal thoracic veins

(f) Nerve Supply Nerve supply of the pericardium is from the phrenic nerve.

The fibrous and parietal layers are sensitive to pain.

The epicardium is supplied by autonomic nerves and is not sensitive to pain.

Applied Anatomy

1. Inflammation of pericardium is called **pericarditis**. It may be dry or fluid may accumulate in the pericardial cavity, which is called **pericardial effusion**.
2. Pericardial effusion can be drained by puncturing at the level of the 5th or 6th intercostal space lateral to the apex beat or in the angle between the xiphoid process and the left costal margin.
3. Too much fluid in the cavity can result in pericardial tamponade (compression of the heart within the pericardial sac). A pericardiectomy (surgical removal of the pericardium) is sometimes needed in cases when adhesions lead to constrictions.
4. Pain of pericarditis originates in the parietal pericardium alone.
5. Cardiac pain originates in the cardiac muscle or in the vessels of the heart.

2. Myocardium

Myocardium is the muscular middle layer of the wall of the heart. The bulk of the heart is formed by the myocardium. It is composed of spontaneously contracting specialized cardiac muscles, found only in the heart. It is not under voluntary control. The amount of myocardium and the diameter of muscle fibers in the chambers of the heart vary according to the workload of the chamber. Myocardium is thickest at the apex and thins out towards the base. It is thickest in the left ventricle.

Microscopically, the myocardial fibers appear like cross stripes. Each fiber has a nucleus. It has one or more branches. The end of one cell is in close contact with the end of the adjacent cell. At the places of contact, the membranes of both the adjacent cells fuse to form a tough structure called the **intercalated disc**. So the cardiac muscle appears like a sheet of muscle. Due to end-to-end continuity, each muscle fiber does not need a separate nerve supply. When an impulse is initiated in one cell, it spreads from cell-to-cell via the branches and joints (intercalated discs) causing contraction. This enables the atria and ventricles to contract as a whole in a coordinated and efficient manner.

The atria and ventricles are separated by a ring of fibrous tissue. This fibrous tissue does not conduct electrical impulses. When an electrical wave originates in the SA node, situated in the right atrium, it passes all over the atria and reaches the ventricles through the conducting system which bridges the fibrous ring between atria and ventricles.

3. Endocardium

The endocardium is the inner layer of the heart. It consists of epithelial tissue and connective tissue. It is a thin, smooth, glistening membrane which permits smooth flow of blood inside the heart. It lines the inner cavities of the heart, covers heart valves, and is continuous with the inner lining of blood vessels.

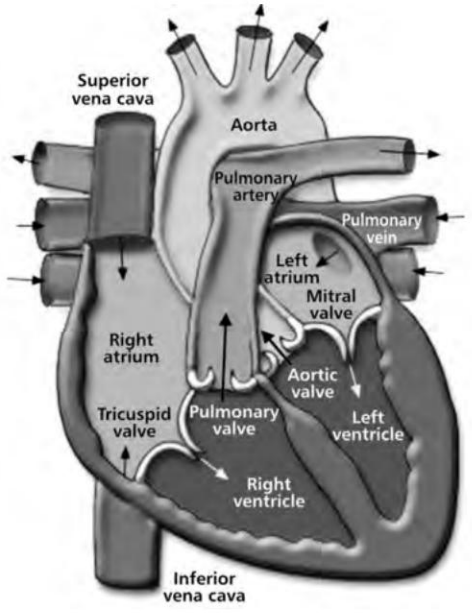


Fig. 7.4 *Valves of the heart (Refer colour figure)*

7.1.3 Interior of the Heart

Heart Valves

Blood is pumped through the four chambers, aided by four heart valves. The valves open and close to let the blood flow in only one direction depending on the difference in pressure on each side.

There are four valves in the heart.

- The two atrioventricular (AV) valves between the atria and the ventricles.
- The two semilunar valves, in the main arteries leaving the heart.

(a) Atrioventricular (AV) Valves The right AV valve is called **tricuspid valve** as it has three cusps.

The left AV valve is called **bicuspid valve** as it has two cusps. This valve is also called the mitral valve.

The cusps are flat and project into the ventricular cavity. There is a fibrous ring to which the cusps are attached.

Each cusp has an attached and a free margin, and an atrial and a ventricular surface. Atrial surface is smooth while the free and ventricular surface is rough and irregular as the chordae tendinae are attached to it.

Chordae tendinae connect the free margins and ventricular surfaces of the valves to the apices of papillary muscles. The AV valves are kept competent by active contraction of papillary muscles which pull on the chordae tendinae during ventricular systole (contraction).

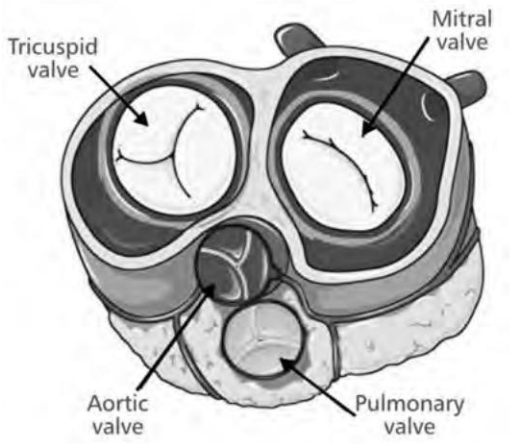


Fig. 7.5 *Valves of the heart (view from above)*

The valves are closed during ventricular systole, by apposition of the atrial surfaces near its serrated margins.

The mitral cusps are smaller and thicker than those of the tricuspid valves.

(b) Semilunar Valves The aortic and pulmonary valves are called semilunar valves because cusps are semilunar (half-moon) in shape. Both the valves are similar in shape.

Each valve has 3 cusps and is directly attached to the vessel wall as there is no fibrous ring.

These valves close, and each cusp bulges into the ventricular cavities during ventricular diastole. They open during the ventricular systole.

Opposite the cusps, the vessel walls are slightly dilated. These dilated portions are called sinuses.

There are three aortic sinuses, one anterior and two posterior—right and left.

The coronary arteries arise from the anterior and left posterior aortic sinuses.

(c) Applied Anatomy The valves allow blood to flow through the heart smoothly and prevent it from leaking back against this flow. Valves allow blood to flow in one direction only.

1. The opening and closing of the heart valves produce the sound of the heartbeat. The first heart sound is produced by the closure of AV valves. The second heart sound is produced by the closure of semilunar valves.
2. If a valve becomes narrowed, blood cannot, readily, flow into the next chamber or blood vessel. This is called **valve stenosis**. Narrowing of a valve orifice could be due to fusion of cusps, e.g., mitral stenosis or aortic stenosis.
3. If a valve doesn't close properly, blood leaks backwards in the wrong direction. This is called **valve insufficiency** or incompetence, e.g., mitral regurgitation or aortic regurgitation.

Both valve stenosis and valve incompetence put extra strain on the heart.

Heart-valve surgery is used to repair or replace diseased heart valves.

7.1.4 Blood Vessels

The heart pumps blood into the vessels that vary in structure, size and function.

The main types of blood vessels are arteries, arterioles, capillaries, venules and veins.

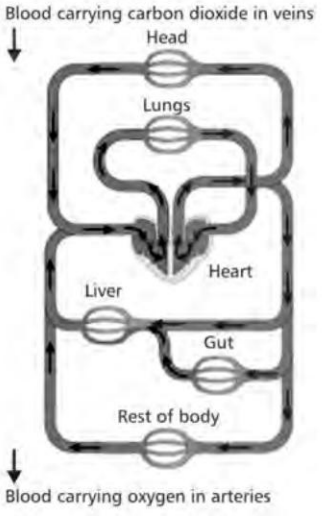


Fig. 7.6 *Circulation of blood*

1. Arteries and Arterioles

The arterial system is divided into systemic arteries, carrying oxygen-rich blood from the heart to the whole body, and pulmonary arteries, carrying deoxygenated blood from the heart to the lungs.

Structure The outermost layer is known as the **tunica externa,** also known as **tunica adventitia,** and is composed of fibrous connective tissue. Inside this layer is the **tunica media,** which is made up of smooth muscle cells and elastic tissue. The innermost layer, which is in direct contact with the flow of blood, is the **tunica intima.** This layer is made up of mainly endothelial cells. The hollow internal cavity in which the blood flows is called the **lumen.**

Muscular elastic tissue varies depending on the size of the arteries.

In large arteries, the tunica media consists of more elastic tissue and less smooth muscle. Arteries branch many times. A smaller artery is called an arteriole. In arterioles, the tunica media consists only of smooth muscle. Arteries have thicker walls than veins.

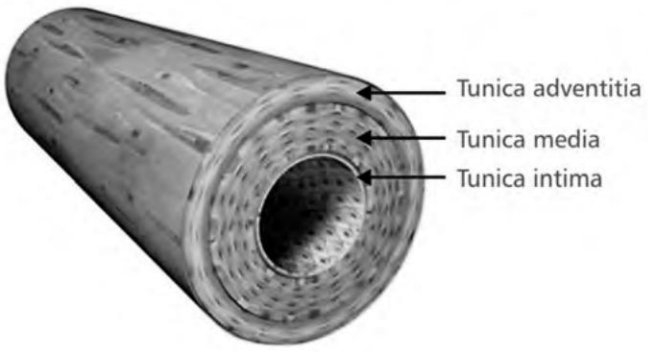


Fig. 7.7 *Artery anatomy*

The aorta is the main artery which receives blood directly from the left ventricle. The aorta branches into arteries which in turn branch and become successively smaller in diameter, down to the arteriole. The arterioles supply capillaries, which in turn empty into venules.

Contractions of the smooth muscle of the walls of arterioles deliver blood to the capillaries and also help in maintaining the level of blood pressure.

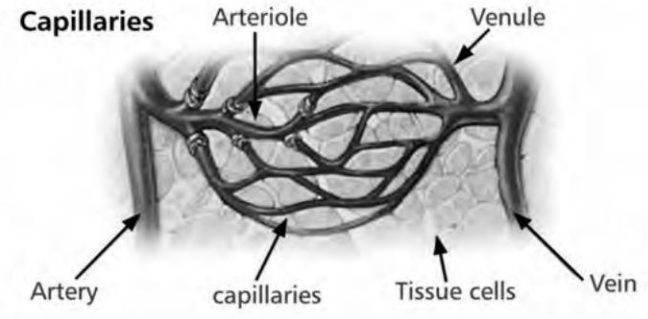


Fig. 7.8 *Site for exchange of gaseous and other metabolites (Refer colour figure)*

2. Capillaries and Sinusoids

The gaseous exchanges take place at the level of capillaries. The capillaries are the smallest blood vessels in the body, about a single cell in diameter, and so there is fast and easy diffusion of gases, sugar and other nutrients to the surrounding tissues.

Capillaries are the link between the arterioles and venules which allow the transfer of substances to occur. The very thin walls of the capillaries allow nutrients and gases to diffuse into the cells and waste products from the cells (i.e., carbon dioxide) to diffuse back in the blood for removal. Blood cells and large molecular substances cannot pass through this layer. Different tissues will have different amounts of capillaries depending upon the individual tissue's demand for oxygen and nutrients. Capillaries form a vast network of tiny vessels, linking the smallest arterioles to smallest venules.

Diameter of capillaries is 7μm, i.e., the diameter of an RBC.

Sinusoids are wider than capillaries. They have extremely thin walls separating blood from the tissue cells. Blood pressure in sinusoids is lower than that in the capillaries. There is slower rate of blood flow because of larger lumen.

Sinusoids have functions that are greatly similar to the capillaries in which they are directly involved in the transfer of substances between the blood and the body cells. Sinusoids are usually found in the liver, spleen and the bone marrow. They are composed, mostly, of endothelium and have a diameter of 30–40 microns.

3. Anastomosis and End Arteries

The branches of different arteries form a link between the main arteries. These branches are called anastomoses, e.g., palm of hand, sole of feet, brain, heart, etc. So if one artery is blocked, anastomotic arteries provide collateral circulation. Good blood supply can be provided if the occlusion is gradual as it gives time for the anastomotic arteries to dilate.

End arteries are arteries with no anastomoses, e.g., the central artery of retina or the circle of Willis. When an end artery gets occluded, the tissue supplied by it dies as there is no alternative blood supply.

4. Arterial System

The aorta is the main artery arising from the upper part of the base of the left ventricle. This is called **ascending aorta**. It then forms an arch called the **arch of aorta**. The branches arising from the arch are innominate, left common carotid and left subclavian. The **innominate** divides into right common carotid and right subclavian arteries.

It then descends within the thorax on the left side of the vertebral column as the thoracic aorta. Then it passes into the abdominal cavity—as abdominal aorta—through the aortic hiatus in the diaphragm, and ends at the level of the fourth lumbar vertebra by dividing into the right and left common iliac arteries.

The iliac arteries pass into the lower limbs to divide into internal iliac and external iliac arteries. The external iliac artery runs downwards as the **femoral artery** in the thigh and as the **popliteal artery** in the popliteal region. The popliteal artery divides into anterior and posterior tibial arteries in the leg and gives rise to the pedis arteries and planter arteries in the foot. (See Fig. 7.9)

5. Veins and Venules

Blood flows from the capillaries into very small veins called venules, then into the veins that lead back to the heart. Veins have three layers of tissue just as in the arteries but they have

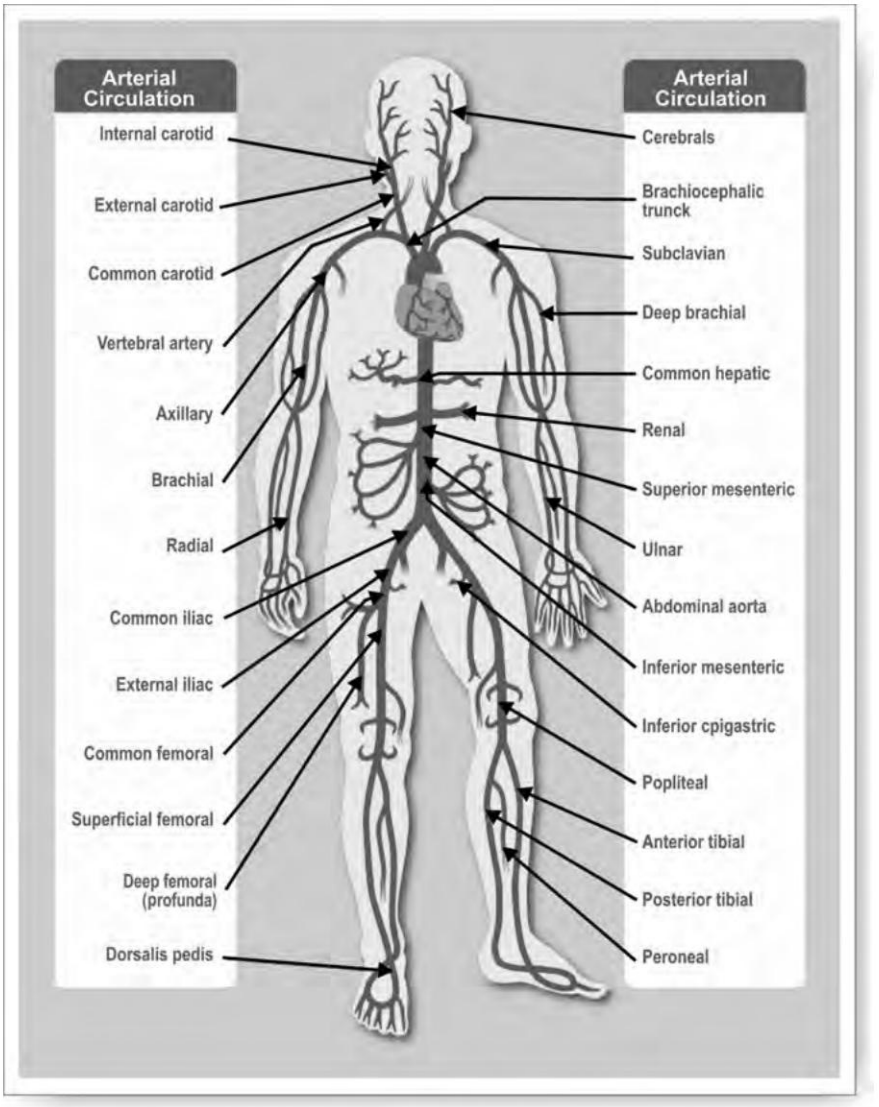


Fig. 7.9 *Arterial system of the human body*

much thinner walls. This is because there is less muscle and elastic tissue in the tunica media and also, because the pressure in veins is much low. Veins can widen (dilate) as the amount of fluid in them increases. Some veins, particularly veins in the legs, have valves in them, to prevent blood from flowing backwards. Valves are plenty in the limbs, especially the lower limbs, where blood has to travel a long distance against gravity. Valves are absent in very small veins and in the very large veins in the thorax and the abdomen.

6. Venous System

The venous system is responsible for returning the blood to the heart after exchanges of gases, nutrients and wastes have occurred between the blood and body cells.

Blood from the head, neck, face, upper limbs and some part of the thorax is returned to the right atrium through the superior vena cava which is formed by two brachiocephalic veins.

Internal jugular, external jugular and subclavian veins unite to form respective brachiocephalic veins. They bring blood from the brain, neck and face.

In the upper limb, various veins join to form the palmer arch. The radial and ulnar veins join with the veins of the upper arm. In the upper arm, the brachial, cephalic and basilica veins unite to form the axillary vein which drains into the subclavian vein.

The **inferior vena cava** is formed by the union of two common iliac veins which is formed by the union of external and internal iliac veins. The inferior vena cava drains blood from the lower extremities and abdomen. It passes through the abdomen and thorax and opens into the right atrium.

Blood from the foot is collected by the **dorsal arch**. From the foot, the great saphenous vein drains into the femoral vein.

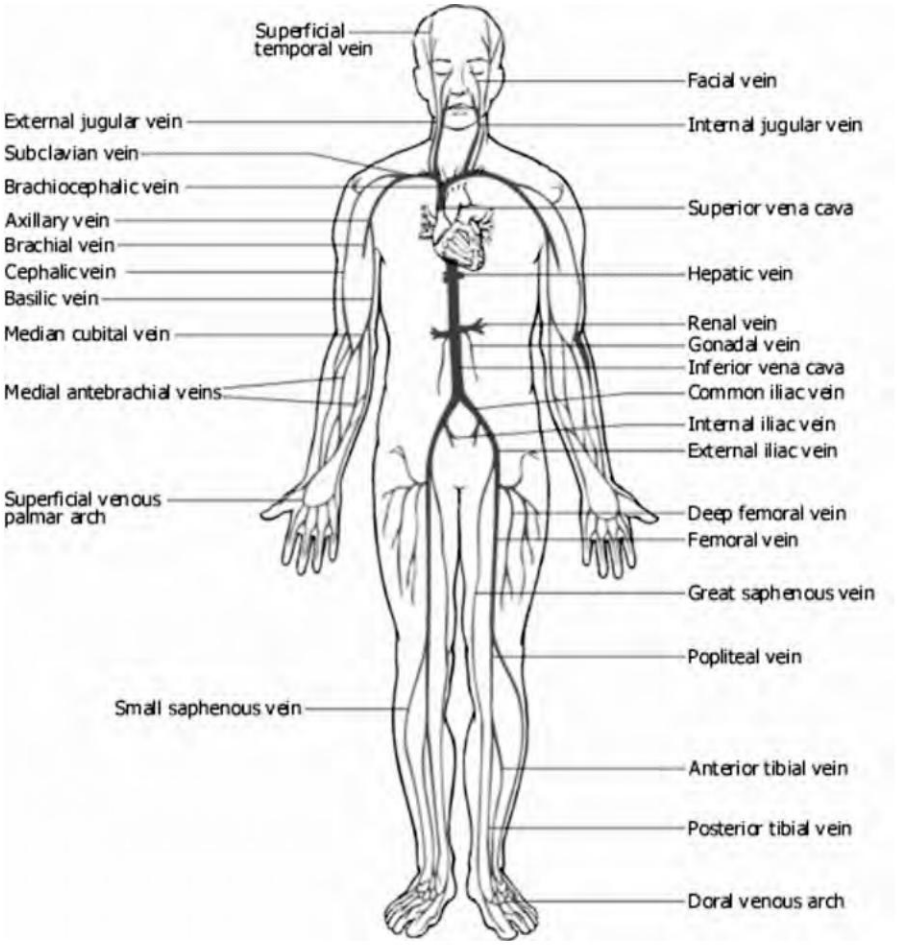


Fig. 7.10 *Venous system of the human body*

Table 7.1 *Difference between arteries and veins*

Artery	*Vein*
Walls are thicker as they have more muscle tissue	Walls are thinner as there is less muscle tissue
Transport blood away from the heart	Transport blood towards the heart
When cut they remain open	When cut they collapse
Blood spurts at high pressure when cut	Blood flows slowly when cut
Do not have valves	Have valves in some veins especially in the lower limb veins
Carry oxygenated blood except pulmonary artery	Carry deoxygenated blood except pulmonary vein
Have relatively narrow lumen	Have relatively wide lumen
Smallest artery is capillary	Smallest vein is venule
Transport blood under high pressure	Transport blood under lower pressure

Anterior and posterior veins join to form the popliteal vein which forms the **femoral vein**. The femoral vein continues as the external iliac vein.

Azygos and hemiazygos drain into inferior vena cava in the thorax. In the abdomen, it receives renal veins, suprarenal veins, gonadal veins, lumbar veins, hepatic veins and internal and external iliac veins. (See Fig. 7.11)

7.2 PHYSIOLOGY

To understand the various properties of the heart muscles, it is necessary to know about the conducting system of the heart.

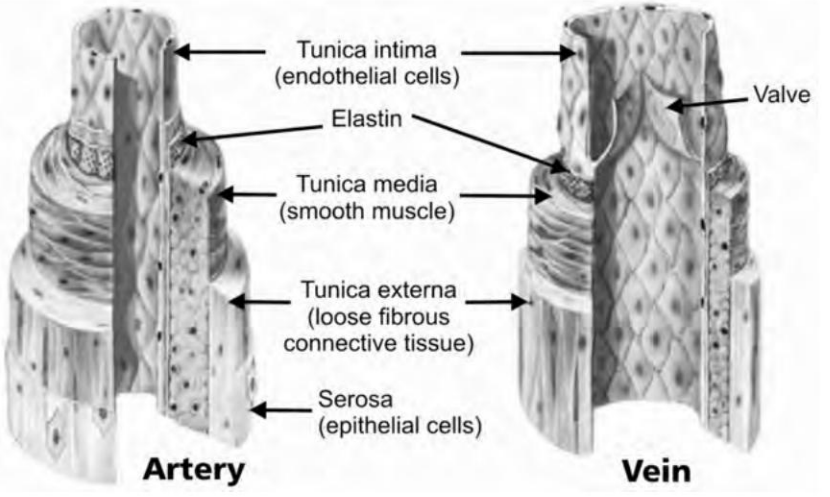


Fig. 7.11 *Artery and vein*

7.2.1 Conducting System of the Heart

The heart's conducting system consists of the Sino Atrial node (SA node), Atrio Ventricular node (AV node), and the bundle of His, the right and the left bundle branches and the Purkinje fibers.

The electrical impulse that causes rhythmic contraction of heart muscles arise in the SA node which is the intrinsic pacemaker of the heart. From the SA node, the impulse spreads over the atrial muscles causing atrial contraction. The impulse is also conducted to the AV node.

From the AV node, the electrical impulse is conducted to ventricular muscles via the bundle of His, the bundle branches and the Purkinje fibers. The bundle branches and the Purkinje fibers are collectively called the ventricular conduction system.

1. SA Node

The sinoatrial node (SA node) consists of a cluster of specialized cells in the wall of the right atrium, near the opening of superior vena cava that has a pacemaker activity (automaticity) and hence, it is called the pacemaker of the heart. It initiates impulses more rapidly than other groups of neuromuscular cells (viz., AV node). These cells are responsible for initiating the electrical impulse that stimulates the heart muscles to contract rhythmically.

The cells here are in continuity with the fibers of the atrial muscle, so that impulses generated from the SA node can spread rapidly to the atria. Other parts of the heart, viz., AV node, atria, ventricles can produce impulses, but at a slower rate.

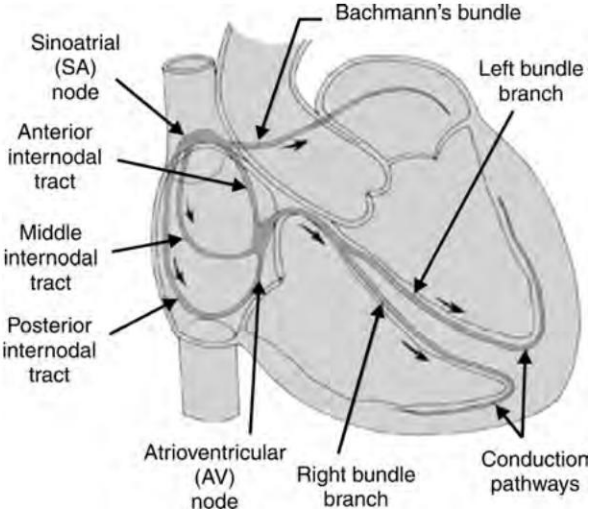


Fig. 7.12 *Electrical system of the heart*

Impulses from SA node are conducted to AV node by means of 3 bundles of atrial fibers:

- Anterior internodal fibers
- Middle internodal fibers
- Posterior internodal fibers

2. AV Node

The AV node is a small mass of neuromuscular tissue, situated in the wall of the atrial septum, on the right side, near the AV valves.

Normally, the AV node is stimulated by impulses coming from the atrial myocardium but it can also generate its own impulse and can make the heart contract but the rate is slower than the SA-node rate.

3. Bundle of His

The bundle of His is a small mass of specialized fibers originating from the AV node.

This bundle crosses the fibrous ring separating the atria from the ventricles.

At the upper end of the ventricular septum, it divides into two branches, the right and the left bundle branch.

In the ventricular myocardium these branches break into fine fibers called **Purkinje fibers**.

AV bundle, bundle branches and the Purkinje fibers, all convey impulses from the AV node to the apex of the myocardium, where a wave of contraction starts which sweeps upwards and outwards, pumping blood into the pulmonary artery and aorta, from the right ventricle and left ventricle respectively.

The velocity of conduction is maximum in the Purkinje fibers and minimum in the AV node.

7.2.2 Properties

The cardiac muscle has four basic properties, namely,

- Excitability
- Rhythmicity
- Conductivity
- Contractility

1. Excitability

The ability of a tissue to respond to a stimulus is called excitability. The heart muscle cell membrane is an excitable membrane, i.e., it is capable of transmitting an action potential. In individual cardiac-muscle fiber, the resting potential is about –85 mV to –95 mV. It is different from electrocardiogram.

The unique characteristic of cardiac-muscle action potential is the plateau phase, i.e., the maintenance of the potential at a positive level. This plateau is due to slow sodium and calcium channels which remain open for some time.

Approximate duration of the action potential is 250 to 350 ms (0.25 to 0.35 s).

The depolarization is very rapid (2 ms) which is due to rapid opening of sodium channels and rapid influx of sodium ions.

Repolarization is produced by the closing of the fast sodium channels and opening of the chloride ions. Because of this, the muscle remains in the depolarized state for some time. This forms the plateau in the action-potential curve. Prolonged depolarization ensures that the Absolute Refractory Period (ARP) of the heart muscle cells is relatively longer than that of other muscle cells. This is important for normal pumping action of the heart; it requires some component of the diastolic period to get filled with blood.

This is due to slow and prolonged opening of calcium channels. The calcium ions entering the muscle fiber play an important role in the contractile process.

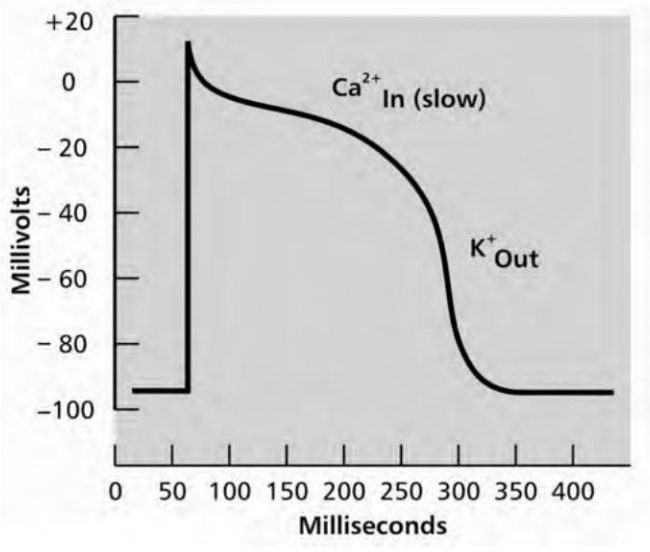


Fig. 7.13 *Action potential*

The final slow repolarization is due to closure of calcium channels and prolonged opening of potassium channels.

The action potential spreads through the cardiac muscle very rapidly from one muscle fiber to another fiber and it is transmitted from atria to ventricles through the fibers of the specialized conductive system.

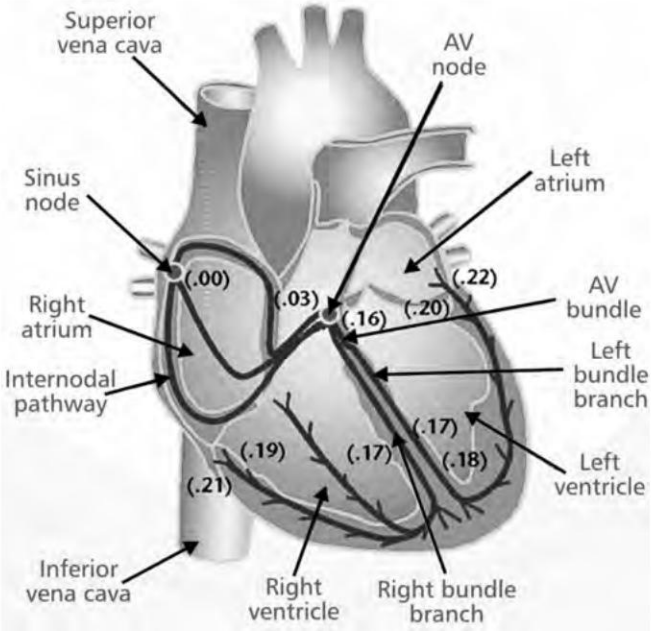


Fig. 7.14 *Spread of action potential*

2. Rhythmicity

The ability of a tissue to produce its own impulses regularly is called rhythmicity or autorhythmicity. This property is possessed by all the tissues of the heart. But the pacemaker has maximum rhythmicity.

Besides the SA node, the other parts of the heart also can produce impulses.

Normal rhythmicity of each tissue:

- SA node 70 to 80/min
- AV node 40 to 60/min
- Atrial muscle 40 to 60/min
- Ventricular muscle 20 to 40/min

The electrical potential in SA node is different from that of other cardiac muscle fibers. In the SA node, each impulse triggers the next impulse and is due to unstable resting membrane potential.

3. Conductivity

In the human heart the impulses produced by the SA node are transmitted to the cardiac muscle by means of a specialized conductive system. As mentioned before, it starts with the SA node. The impulse then goes through the atrial fibers to the AV node, bundle of His, bundle branches and finally the Purkinje fibers, and leads to the contraction of the heart. This conductivity goes on and on automatically and the heart beats rhythmically.

4. Contractility

Contractility is defined as the intrinsic ability of a cardiac-muscle fiber to contract at a given fiber length, or it can be defined as the ability of the cardiac-muscle fiber to shorten in length (contraction) after receiving a stimulus.

Various factors affect the contractile properties of the cardiac muscle. If a stimulus is applied, whatever the strength, the muscle responds to the maximum or not at all. This is called **all-or-none law**. The whole cardiac musculature responds in this way.

When a stimulus of subliminal strength is applied to the heart then the heart shows no response. But when a few stimuli with the same subliminal strength are applied, there is contraction of the heart. This is due to **summation of stimuli**.

When stimuli are applied to the base of the ventricle of a frog, at 2-second intervals, without changing the strength, for the first few contractions the force is gradually increased and then the force of contraction remains the same. This is due to the time interval of 2 seconds between the stimuli, which produces a beneficial effect. This is called **staircase phenomenon** because successive contractions are facilitated and rise occurs.

The **refractory period** is the period when the heart does not show any response to stimulus. **Absolute refractory period** is the period during which the heart does not show any response to a stimulus, whatever the strength of stimulus. During **relative refractory period**, the muscle responds if the strength of stimulus is increased to maximum.

7.2.3 Cardiac Cycle

The function of the heart is to maintain a constant circulation of blood flow throughout the body. The heart acts as a pump. The various actions during pumping of the heart give rise to a series of events known as the cardiac cycle.

Each pump or beat of the heart consists of two parts or phases—diastole and systole. During **diastole** the ventricles are relaxed and get filled with blood and the atria contract. During **systole**, the ventricles contract and pump the blood into great vessels while at this time the atria are relaxed and are getting filled up with the blood.

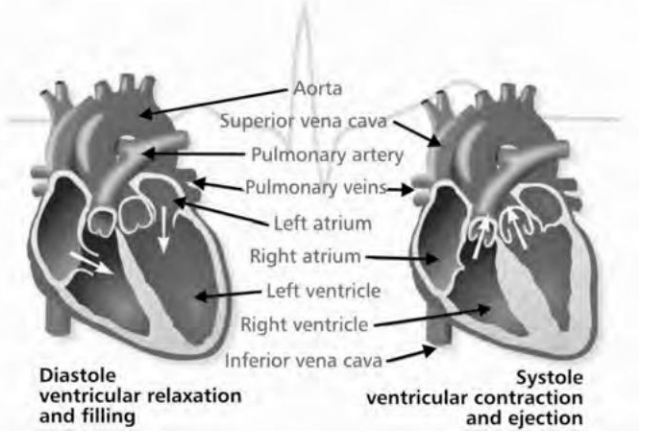


Fig. 7.15 *The cardiac cycle (Refer colour figure)*

Various changes occur in the different chambers of the heart during each heart beat and these changes are repeated in a cyclic manner. The normal number of cardiac cycles is 60 to 80 per minute.

Phases of Cardiac Cycle

Each cardiac cycle is described as having the following phases:

- Atrial systole
- Isovolumic ventricular systole
- Ventricular ejection
- Isovolumic ventricular relaxation
- Rapid ventricular filling
- Diastasis
- Last rapid filling phase or atrial systole

The right atrium gets filled with deoxygenated blood through the superior vena cava and inferior vena cava at the same time as the four pulmonary veins fill up oxygenated blood into the left atrium. The AV valves open and blood flows into the ventricles.

The spontaneous generation of an action potential within the SA nodal tissue represents the start of the cardiac cycle. This electrical impulse spreads throughout the atrial muscle and

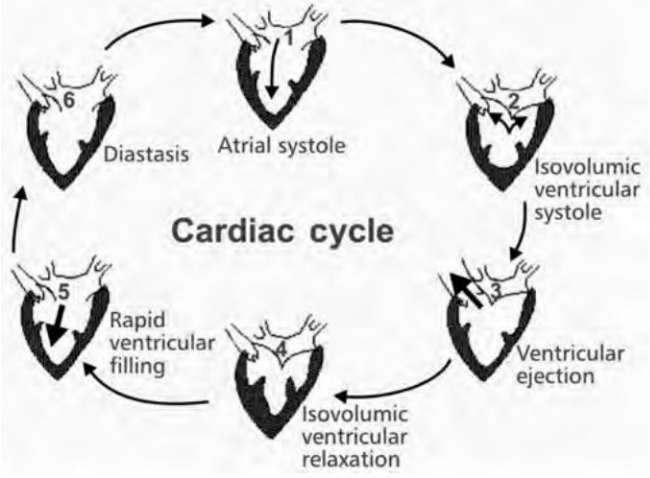


Fig. 7.16 *Phases of the cardiac cycle*

leads to contraction of the two atria. This is the atrial systole. Even before the atria contract, the ventricles are filled with blood to approximately 70% of their capacity. When the atria do finally contract, additional blood enters the ventricles and elevates the intraventricular pressure.

Immediately after the atrial systole, AV valves close. Semilunar valves are already closed. Now the AV node is stimulated and impulse spreads to ventricular muscle via AV bundle, bundle branches and Purkinje fibers. Ventricles contract as closed cavities, with no change in the volume of its chambers and so pressure inside increases sharply; this is **isovolumic ventricular systole**.

Ventricles contract because the pressure within them soon exceeds that in the aorta and the pulmonary trunk, semilunar valves open and blood is pumped into these great vessels. High pressure is generated in the ventricles, so the AV valves get closed preventing backflow of blood into the atria. This is the ventricular systole, also described as **ventricular ejection**.

After contraction of ventricles, there is complete cardiac diastole when both atria and ventricles are relaxed. This period lasts for 0.4 second and is called **isovolumic relaxation**. During this period, again all the valves are closed. Both ventricles relax as closed cavities without change in volume. (See Fig. 7.17)

With the opening of the semilunar valves there is a rapid decline in intraventricular pressure which continues until the pressure within the ventricles becomes less than that of the atria. Blood within the atria pushes the AV valves open and begins to fill the ventricles once again. This is rapid ventricular filling. After rapid rush of blood, ventricles fill slowly. This is **diastasis**.

After slow filling period, atria contract and the cycle is repeated. The atrial systole is also called the last rapid filling phase and a small quantity of blood enters from atria into ventricles.

The valves of the heart and great vessels open and close according to the pressure within the heart chambers.

AV valves open during atrial filling and when the ventricles are relaxed. When ventricles contract, pressure gradually increases within the ventricles and when this pressure rises above atrial pressure, the AV valves close and semilunar valves open.

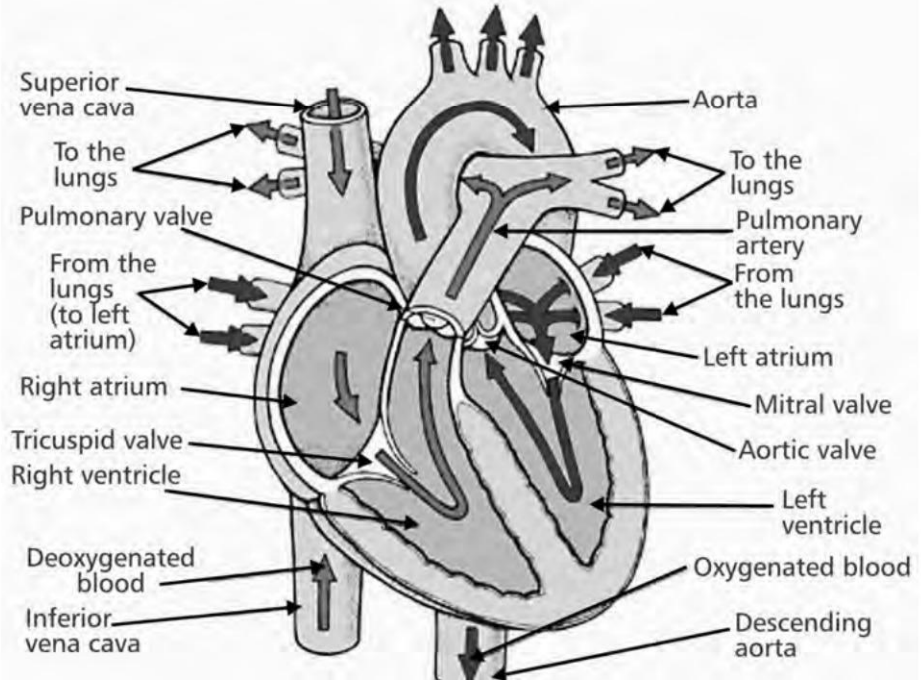


Fig. 7.17 *Cardiac cycle—blood flow*

This sequence of opening and closing of valves ensures that the blood flows in only one direction.

Intra-atrial pressure is essential to open the AV valves and ventricular filling. It is also the main factor causing the development of venous pulse.

Maintenance of blood flow into systemic and pulmonary circulation depends upon the pressure at which blood is pumped out of the ventricles. So, intraventricular pressure is essential for the circulation of blood.

Each cardiac cycle is of 0.9 second, of which the systole occupies 0.4 second and the diastole occupies 0.5 second.

7.3 HEART SOUNDS

The Heart Sounds (HS) are the sounds generated by the beating heart and the resultant flow of blood through it. They give an idea of the mechanical activities of the heart during each cardiac cycle.

Normally, an individual is not conscious of his own heartbeat, but if he places the diaphragm of a stethoscope on the left side of the chest wall over the area of the heart, the heart sounds can be heard.

Four sounds are produced during each cardiac cycle, of which the first and second heart sounds are more prominent and spoken of as 'lubb-dup'.

In addition to these normal sounds, a variety of other sounds may be present including heart murmurs and adventitious sounds.

1. The First Heart Sound or S1

The first heart sound or S1 produces the sound 'lubb' of 'lubb-dup'. It is caused by the sudden closure of both atrioventricular valves, at the beginning of ventricular contraction. Some other factors are also involved, e.g., when the ventricles begin to contract, the papillary muscles in each ventricle, which are attached to the tricuspid and mitral valves via chordae tendinae, also vibrate and contribute to the production of first heart sound. Residual vibrations produced by atrial systole also are responsible.

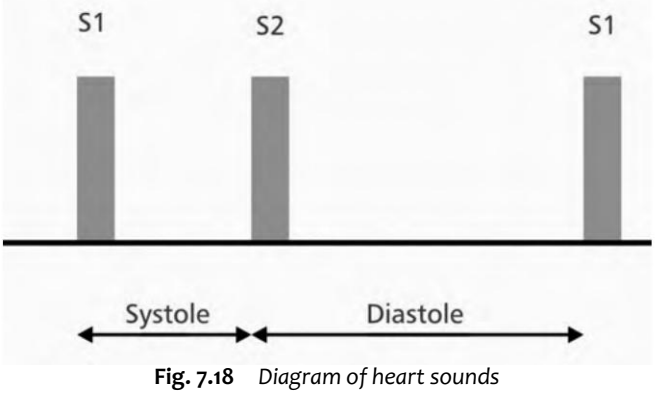


Fig. 7.18 *Diagram of heart sounds*

The first sound is normally lower in pitch than the second sound.

First HS coincides with peak of 'R' wave in ECG.

2. The Second Heart Sound or S2

The second heart sound, or S2, produces the sound 'dup' of 'lubb-dup'. It is a short, sharp, high-pitched sound, which is caused by the sudden closure of the semilunar valves of the aorta and pulmonary artery at the end of the ventricular systole, i.e., beginning of ventricular diastole.

The second heart sound coincides with the 'T' wave in ECG.

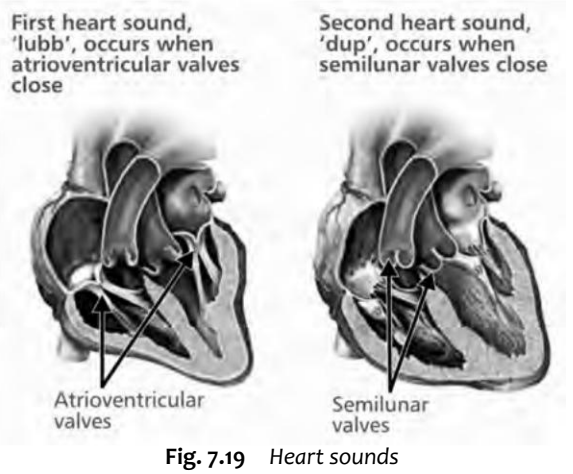


Fig. 7.19 *Heart sounds*

3. The Third Heart Sound or S3

It is a rare extra heart sound that occurs soon after the normal two 'lubb-dup' heart sounds (S1 and S2). It occurs at the beginning of diastole, approximately 0.12 seconds after S2. S3 is normal in people under 40 years of age and some trained athletes but normally disappears before middle age. Re-emergence of this sound, late in life, is abnormal and may indicate serious problems like heart failure. The sound of S3 is lower in pitch than the normal sounds.

S3 is thought to be caused by the oscillation of blood back and forth between the walls of the ventricles, initiated by inrushing blood from the atria.

It has also been termed a **ventricular gallop** or a **protodiastolic gallop**, because of its place in early diastole and because of its typical cadence resembling the sound of hoofbeats of a horse.

4. The Fourth Heart Sound or S4

The rare fourth heart sound is sometimes audible in healthy children and again in trained athletes. This is produced by the sound of blood being forced into a hypertrophic ventricle and is a sign of a pathologic state.

It is called a **presystolic gallop** or **atrial gallop**.

The combined presence of S3 and S4 creates a **quadruple gallop**. At rapid heart rates, S3 and S4 may merge to produce a **summation gallop**.

5. Murmurs

Murmurs are abnormal heart sounds that are produced as a result of turbulent blood flow which is sufficient to produce audible noise. This, most commonly, results from narrowing or leaking of valves or increased blood flow or the presence of abnormal passages through which blood flows in or near the heart. Murmurs are not usually part of the normal cardiac physiology and thus warrant further evaluation for its cause.

6. Adventitious Sounds

With the advent of newer, non-invasive imaging techniques, the origin of other, so-called adventitial sounds, e.g., clicks, opening snap, mid-systolic click, etc., have been appreciated. A pericardial friction rub is also diagnostically a very important sound, the presence of which denotes infection or injury of pericardium (external coverings of the heart).

7.3.1 Methods of Studying Heart Sounds

Heart sounds are normally heard by placing the diaphragm of the stethoscope on the anterior chest wall on the left side. Other methods of studying HS are microphone and phonocardiogram.

7.3.2 Applied Physiology

1. The study of heart sounds has important diagnostic value in clinical practice.
2. Heart sounds are altered during diseases that involve the valves of the heart and the ventricles.

7.4 PULSE

7.4.1 Arterial Pulse

Arterial pulse is defined as the rhythmic expansion and contraction of an artery caused by the impact of blood pumped by the heart (left ventricle).

One can get a lot of information from palpation of the arterial pulse. Rate, rhythm, force, volume, contour, tension and bilateral symmetry of the pulse reflect various aspects of the heart function and circulation.

In most people, the pulse is an accurate measure of heart rate. The pulse rate can be measured by examining the pulse clinically (usually at the wrist). Pulse rate may also be obtained using a pulse oximeter.

When the heart contracts, blood is ejected into the aorta and the aorta stretches. At this point, the wave of distention travels along the walls of the peripheral blood vessels, which is felt as the pulse. It can be palpated in any place that allows for an artery to be compressed against a bone, such as at the wrist (radial artery), at the neck (carotid artery), at the groin (femoral artery), behind the knee (popliteal artery), on the inside of the elbow at cubital fossa (brachial artery), and near the ankle joint (posterior tibial artery).

The normal pulse rate is 60 to 80 per minute. In the large arterial branches, the velocity is 7–10 m/s; in the small arteries, it is 15–35 m/s. The pressure pulse is transmitted fifteen or more times more rapidly than the blood flow.

Pulse is manually palpated with the fingers. The most traditionally used pulse site is the radial artery which is located on the lateral edge of each wrist. It is easily accessible and is convenient to the doctor as well as the patient.

The external carotid pulse can be palpated on either side of the neck between the trachea and the anterior border of the sternomastoid muscle. Take care not to apply too much pressure over it so as to prevent cerebral ischemia and also to prevent a vaso-vagal reflex which can result in a sudden drop in blood pressure and heart rate. Also both the carotid arteries should not be palpated simultaneously.

Three fingers should be used. Fingers must be placed and pressed gently against a firm structure, usually a bone, in order to feel the pulse. It should be counted for one minute.

1. Pulse Waves

There are two limbs in the arterial pulse:

1. Ascending limb
2. Descending limb

The ascending limb is the primary wave and is called the **anacrotic limb**. It is a smooth, rapid upstroke with a smooth dome-shaped summit. It is caused by the rise in pressure during systole.

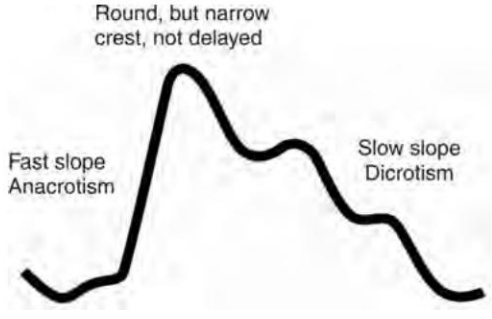


Fig. 7.20 *Normal curve shape of pulse waves*

The descending limb is called the **dicrotic limb** and is caused due to fall in pressure during diastole. It is somewhat less rapid than the upstroke.

In the upper part of the dicrotic limb, there is a small notch known as **dicrotic notch**. This is produced by the backflow of blood during the closure of semilunar valves. The dicrotic notch and secondary diastolic wave are usually not felt but can be palpable in some normal individuals, particularly during fever, exercise, or excitement.

The pulse rate is measured by counting or calculating the pulsations for 60 seconds. The average rate is 72 beats per minute with a normal range of 60–80 beats per minute. The rhythm of the pulse should be regular and bilaterally equal at each wrist. Although the pulse rate is usually the same as the heart rate, if the patient is in shock, pulse maybe hardly felt (feeble) or in conditions where there are extra beats, some of them may not be conducted to the radial pulse.

A change in rhythm (irregularity) could indicate heart disease or a conduction system disorder. However, in sinus arrhythmia (a physiological condition), pulse rate cyclically increases during inspiration and decreases during expiration.

Should pulse be unequal, this would indicate a possible vascular disorder on one side, i.e., the side where the pulse is weak. The intensity of the femoral and radial pulses should also be roughly equal.

The contour of the pulse wave is normally rounded and dome-shaped. As the pulse is measured with three fingertips, an assessment can be made of the ascending portion, the crest and the descending portion of each wave. This can help infer the etiology of an existing problem. The amplitude of a pulse wave can be graded on a scale from 0–4, where

0 = absent
1 = barely palpable
2 = average intensity
3 = strong
4 = bounding

2. *Pulse Variants*

(a) Regularly Irregular Pulse After one normal beat, an extra beat is noted, followed by a compensatory pause. Again, this pattern is repeated. This is called **bigeminy**. Similarly, every third or fourth beat may be an extra beat, called **trigeminy** or **quadrigeminy** respectively.

(b) Irregularly Irregular Pulse In this type of pulse, the beats come irregularly and the intervals between two beats are also irregular. The amplitude of each beat varies with the filling interval. This is found in various cardiac arrhythmias. Cardiac dysrhythmias are capable of producing some contractions that are sufficient to produce a palpable pulse wave and some that are not.

(c) Bounding Pulse It is a hyperkinetic pulse with a rapid large-amplitude upstroke and rapid collapse. The classic collapsing pulse (a rapid and snapping pulse) is found in pregnancy, fever, and anemia and in certain cardiac diseases.

(d) Pulsus Paradoxus Normally, during inspiration there is mild decrease in volume of the pulse, and during expiration it increases. It is rarely noticed. When it becomes prominent, it is pathological.

Other arterial pulse variants like bigeminal pulse, pulsus alternans, thready pulse, water hammer pulse, etc., when observed, are suggestive of pathological heart conditions.

7.4.2 Venous Pulse

Venous pulse is normally observed in the large veins near the heart, and the jugular vein is the chief vein where it is best seen. Analysis of the jugular venous pressure provides information regarding hemodynamic changes in the right side of the heart. The pressure changes which take place in the right atrium during each cardiac cycle are reflected in the form of waves in the jugular vein in the neck.

Factors influencing the right atrial and Central Venous Pressure (CVP) include total blood volume, the distribution of blood volume, and right atrial contraction.

The jugular vein pulse is

1. Not palpable
2. Obliterated by pressure
3. Characterized by a double waveform
4. Varies with respiration—decreases with inspiration
5. Enhanced by the hepatojugular reflux

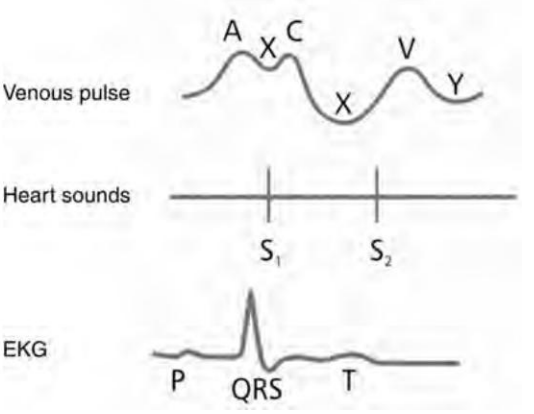


Fig. 7.21 *Venous pulse, heart sounds and EKG*

The normal jugular venous pulse wave or right-atrial pressure wave recordings usually consist of three positive waves, (*a*, *c* and *v*), and two negative waves, (*x* and *y*).

The positive ***a* wave** is caused by the right atrial pressure transmitted to the jugular vein during right atrial systole and before the onset of ventricular ejection (carotid pulse upstroke).

The ***x* wave** is a negative wave that occurs in the late systole. Right atrial relaxation appears to be the primary mechanism, although downward displacement of the tricuspid valve during

right ventricular ejection, which causes a fall in right atrial pressure, also contributes.

The ***c* wave** is recognized with the onset of right ventricular systole and occurs from bulging of the tricuspid valve into the right atrium and increases the pressure in the atria. It is also thought to be due to transmission of the adjacent carotid artery pulsation. The *c* wave of the jugular venous pulse generally cannot be identified separately by clinical examination; recording of the jugular venous pulse is required.

The mechanism of the ***v* wave** is the rise in right atrial and jugular venous pressure due to filling of atria when the tricuspid valve is still closed.

The ***y* descent** is caused by the opening of the tricuspid valve and the rapid inflow of blood to the right ventricle from the right atrium in early diastole. Pressure in the right atrium falls, creating *y* descent.

To summarize, we can conclude in this way.

(a) Waves

1. *a*—presystolic; produced by right atrial contraction
2. *c*—bulging of tricuspid valve into the right atrium during ventricular systole (isovolumic phase)
3. *v*—occurs in late systole; increased blood in right atrium from venous return

(b) Descents

1. *x*—combination of atrial relaxation, downward movement of the tricuspid valve and ventricular systole
2. *y*—tricuspid valve opens and blood flows into the right ventricle

The main aim to study venous pulse is to understand the atrial pressure changes that occur during cardiac cycle. It is also used to determine the rate of atrial contraction.

7.5 FACTORS AFFECTING HEART RATE

There are many factors that affect the rate of the heart.

(a) Autonomic Nervous System The cardiovascular control center for the body is located in the medulla. Heart rate slows if activated by the cardio-inhibitory center in the medulla or speeds up if activated by the cardio-accelerator centers.

The sympathetic components increase heart rate by releasing the neural hormone catecholamines—epinephrine and nor-epinephrine. They are cardio accelerators. Acceleration of the heart rate is called **tachycardia**.

The parasympathetic components decrease the heart rate. These neurons release the neurohormone acetylcholine, which inhibits the heart rate. The slowing of heart rate is called **bradycardia**.

The combination of the neural and chemical components regulates the heart rate and a balance between sympathetic and parasympathetic activity is the most important factor in maintaining the heart rate.

(b) Neural and Hormonal Effects Extrinsic regulation can cause the heart rate to change rapidly because of chemicals (that circulate in the blood) or by direct action of nerves (that go to the heart), e.g., watching a movie or a thrilling scene, can increase the heart rate. There is no cardiovascular or cardiorespiratory change as a result of this alteration in heart rate; it is simply the effect of chemicals and nerves on the heart, responding to an external experience.

(c) Age In babies and small children, the heart rate is more rapid than in older children and adults.

(d) Position of the Body Heart rate is faster in upright position than in the lying-down position.

(e) Exercise Type of exercise is one of the most significant factors responsible for increase in heart rate. The greater the quantity of muscle mass that is used for the exercise, the higher the heart rate that is attained. The highest heart rate is achieved when both upper and lower limb muscle groups are used in the sport, viz., cross-country running. The lowest heart rate during exercise is seen where the body is in a horizontal position, e.g., during swimming.

(f) Drugs and Hormones Adrenaline and noradrenaline secreted by the adrenal medulla have the same effect as in sympathetic stimulation, i.e., they increase the heart rate. Thyroxine hormone increases the heart rate by its metabolic effect.

Drugs such as caffeine, nicotine and cocaine act as stimulants and cause tachycardia, and drugs that are depressants, viz., barbiturates cause bradycardia.

(g) Emotional Stress During excitement, fear, anxiety, the heart rate increases due to activation of the sympathetic nervous system.

(h) Environmental Stress Heart rate is affected by external stresses on the body such as heat, humidity, cold, wind, altitude and air quality. With each stress, the human heart is affected and different compensatory changes occur, one of them being adjustment in the beat of the heart.

(i) Gender Heart rate is more in females as compared to males.

7.6 ELECTROCARDIOGRAM

Electrocardiogram (ECG) is a test that measures the electrical activity of the heart.

The electrical impulses generated, while the heart is beating, are recorded on a special calibrated paper, by attaching electrodes or leads to the surface of the body.

The instrument by which the electrical activities are recorded is called an electrocardiograph.

This machine amplifies the electrical signals from the heart and records them on a moving strip of paper, seen in the form of different waves.

Normally, there are 5 waves	:	*P*, *Q*, *R*, *S* and *T*
Two segments	:	*PR* and *ST* segments
Two intervals	:	*PR* and *QT* intervals

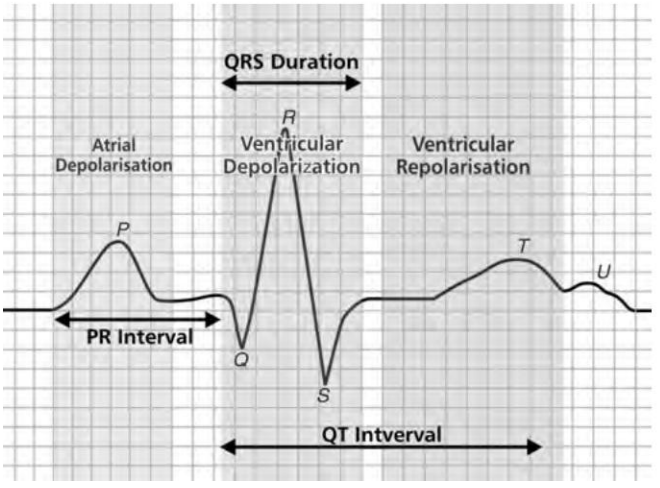


Fig. 7.22 *Normal complex of ECG*

1. 'P' Wave

The *P* wave represents the wave of depolarization that spreads from the SA node throughout the atria, and is usually 0.08 to 0.1 second in duration. It is the first positive wave. The brief period after the *P* wave represents the time in which the impulse is travelling within the AV node and the bundle of His. Atrial rate can be calculated by determining the time interval between *P* waves.

Duration: 0.08–0.1 second.

2. QRS Complex

The *QRS* complex represents ventricular depolarization.

Duration: 0.06–0.1 second.

3. Q Wave

The *Q* wave is a small negative wave and continues as the *R* wave which is a positive wave; this is followed by a small negative wave, the *S* wave.

The *Q* wave is due to depolarization of the basal portion of the interventricular septum.

4. R Wave

The *R* wave is due to depolarization of the apical portion of interventricular septum and depolarization of ventricular muscle. The *R* wave in lead V1-2 represents right ventricular activity. In V5-6, it represents left ventricular activity.

5. S Wave

The *S* wave is due to depolarization of the basal portion of the ventricular muscle. In lead V1-2, the *S* wave denotes left ventricular activity and in V5-6, it represents right ventricular activity.

Ventricular rate can be calculated by determining the time interval between *QRS* complexes. The *R-R* interval is chosen to calculate the heart rate as *R* waves are the tallest recorded waves. It is calculated by dividing 1500 by *R-R* interval.

6. T Wave

The *T* wave is a positive wave and the final ventricular complex. It is due to repolarization of ventricular musculature. It usually takes the same direction as *QRS* complex.

There is no distinctly visible wave representing atrial repolarization in the ECG because it occurs during the phase of ventricular depolarization. Because the wave of atrial repolarization is relatively small in amplitude, it is masked by the much larger ventricular-generated *QRS* complex.

7. PR Segment

It is the time taken by the AV node to conduct the impulse.

8. ST Segment

The isoelectric period (ST segment) following the *QRS* is the time during which the entire ventricle remains depolarized and roughly corresponds to the plateau phase of the ventricular action potential.

9. PR Interval

It is measured from the beginning of the *P* wave to the beginning of *QRS* complex. Actually, it should be termed *PQ* interval but sometimes the *Q* wave is not recorded and hence it is called the *PR* interval.

Duration: 0.12–0.2 second.

10. QT Interval

It is measured from the beginning of *QRS* complex to the end of *T* wave and it represents the electrical systole of the heart.

Duration: 0.44 second.

Thus, each cardiac cycle is represented in the ECG by these waves, segments and intervals.

7.7 CARDIAC ARRHYTHMIAS

Cardiac arrhythmia (also called **dysrhythmias**) is a term for group of conditions, in which there is abnormal electrical activity in the heart. This is a disorder of impulse formation or impulse conduction. The heart beat may be too fast or too slow, and may be regular or irregular. Normally, the heart rate in adults is 60–80 / minute. If the rate is more than 100 or less than 60 / minute, it is called tachycardia or bradycardia respectively.

Some arrhythmias are life-threatening medical emergencies that can result in cardiac arrest and sudden death. Others cause symptoms such as an awareness of heart beat (palpitation), and may be merely annoying. Others may not be associated with any symptoms at all, but predispose towards potentially life-threatening stroke due to embolus.

Some arrhythmias are very minor and can be regarded as variants of normal. In fact, most people will at some time, in their life, feel their heart skip a beat, or give an occasional extra strong beat—neither of which are usually a cause for alarm, especially in young people.

Sinus Arrhythmia

The term 'sinus arrhythmia' refers to a normal phenomenon of mild acceleration and slowing of the heart rate that occurs with breathing in and out respectively. It is usually quite pronounced in children and athletes and steadily lessens with age.

7.7.1 Normal Electrical Activity in the Heart

Each heartbeat originates as an electrical impulse from a small area of tissue in the right atrium of the heart called the SA node. The impulse initially causes both of the atria to contract, and then activates the AV node which is the only electrical connection between the atria and the ventricles (the main pumping chambers). The impulse then spreads through both ventricles via the bundle of His, bundle branches and Purkinje fibers, causing a synchronized contraction of the heart muscle, and thus, the pulse is generated.

7.7.2 Tachyarrhythmia

In adults, the normal resting heart rate ranges from 60 to 80 beats per minute. The resting heart rate in children is much faster.

Any heart rate faster than 100 beats/minute is labeled tachycardia. Tachycardia may result in palpitation; however, it is not necessarily an arrhythmia. Increased heart rate is a normal physiological response to physical exercise or emotional stress. This is mediated by the sympathetic nervous system on the sinus node, and is called **sinus tachycardia**.

Tachycardia (other than sinus tachycardia) usually results from the addition of abnormal impulses to the normal cardiac cycle. Abnormal impulses can begin by one of two mechanisms, viz., automaticity or reentry.

1. Automaticity

Automaticity refers to a cardiac-muscle cell firing off an impulse on its own. Only specialized cells in the heart have the ability to fire off an action potential—these cells are found in the 'conduction system' of the heart that include the SA node, AV node, bundle of His with its two branches and Purkinje fibers. A single specialized location in the atrium, the SA node, has a higher automaticity (a faster pacemaker) than the rest of the heart, and therefore is usually the one to start the heartbeat.

Any part of the heart that initiates an impulse without waiting for the SA node is called an **ectopic focus**, and is by definition a pathological phenomenon. This may cause a single premature beat now and then, or, if the ectopic focus fires more often than the SA node, it can produce a sustained abnormal rhythm.

Conditions that increase automaticity include sympathetic-nervous-system stimulation and hypoxia.

2. Re-entry

Re-entry dysrhythmias occur when an electrical impulse travels in a circle within the heart, rather than moving outward and then stopping. Every cardiac cell is able to transmit impulses in every direction, but will only do so, once within a short period of time. Normally, the impulse spreads through the heart quickly enough so that each cell will only respond once, but if conduction is abnormally slow in some areas, a part of the impulse will arrive late and will be treated as a new impulse, which can then spread backwards. Depending on the timing, this can produce a sustained abnormal rhythm, such as atrial flutter, a self-limiting burst of supraventricular tachycardia, or the dangerous ventricular tachycardia.

3. Fibrillation

When an entire chamber of the heart is involved in a multiple micro-re-entry circuits, there are chaotic electrical impulses, it is called fibrillation.

Fibrillation can affect the atrium (atrial fibrillation) or the ventricle (ventricular fibrillation). Ventricular fibrillation is a very serious, often, terminal, condition unless treated and reverted.

Ventricular fibrillation occurs in the ventricles of the heart; it is always a medical emergency. If left untreated, ventricular fibrillation (VF or V-fib) can lead to death within

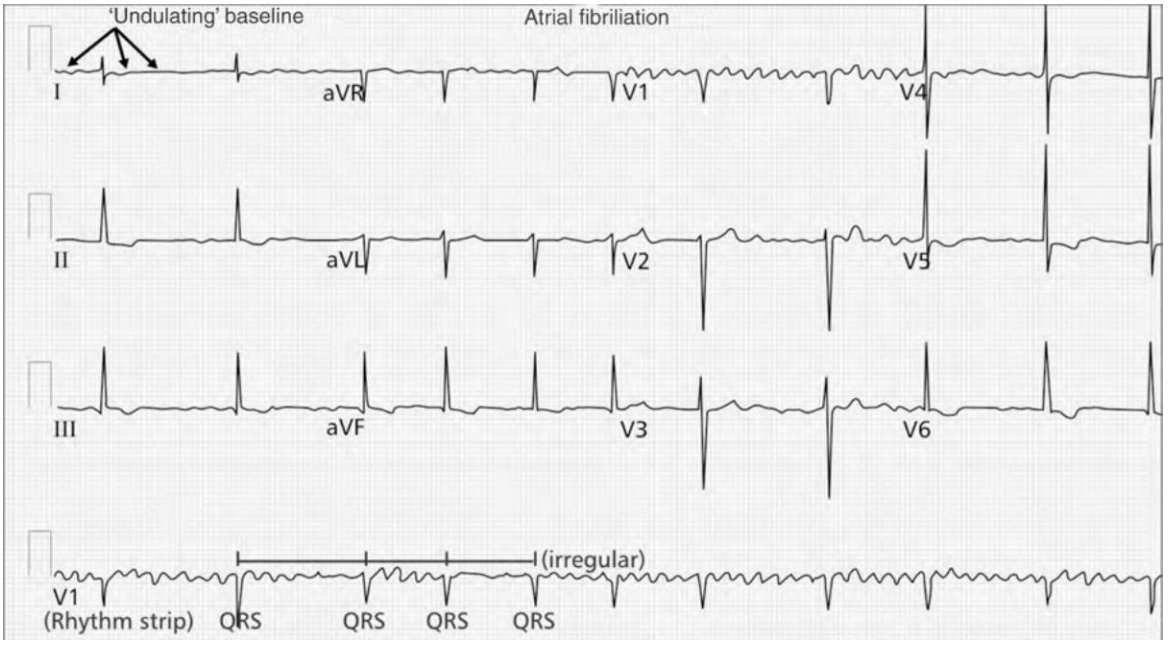


Fig. 7.23 *ECG showing atrial fibrillation*

minutes. When a heart goes into V-fib, effective pumping of the blood stops. V-fib is considered a form of cardiac arrest, and an individual suffering from it will not survive unless Cardio Pulmonary Resuscitation (CPR) and defibrillation are provided instantly.

7.7.3 Bradyarrhythmia

A slow rhythm, (less than 60 beats/min), is labeled as bradycardia. This may be caused by a slowed signal from the sinus node (termed sinus bradycardia), a pause in the normal activity of the sinus node (termed sinus arrest), or by blocking of the electrical impulse on its way from the atria to the ventricles (termed AV block or heart block). Heart block occurs in varying degrees and severity. It may be caused by reversible blocking of the AV node (with drugs that impair conduction) or by irreversible damage to the node.

Symptoms

The commonest symptom of arrhythmia is an abnormal awareness of heartbeat, termed palpitation. These may be infrequent, frequent, or continuous. Some arrhythmias do not cause symptoms, and are not associated with increased mortality. However, some asymptomatic arrhythmias are associated with adverse future events. Examples include increase in the risk of blood clotting within the heart, and thus increase in the risk of embolisation and stroke, or increase in the risk of heart failure, or increase in the risk of sudden cardiac death.

If an arrhythmia results in a heartbeat that is too fast, too slow or too weak to supply the body's needs, this manifests as a lower blood pressure and may cause light-headedness or dizziness or fainting.

Some types of arrhythmia can result in cardiac arrest and sudden death.

Diagnosis

Cardiac dysrhythmias are often first detected by simple but nonspecific means, viz., auscultation of the heartbeat with a stethoscope, or feeling for peripheral pulses. These cannot, usually, diagnose specific dysrhythmias, but can give a general indication of the heart rate and whether it is regular or irregular. Not all the electrical impulses of the heart produce audible or palpable beats; in many cardiac arrhythmias, the premature or abnormal beats do not produce an effective pumping action and are experienced as 'skipped' beats.

The simplest specific diagnostic test for assessment of heart rhythm is the electrocardiogram (abbreviated as ECG or EKG).

A Holter monitor is an ECG recorded continuously over a 24-hour period, to detect burst of dysrhythmias that may have happened briefly and unpredictably in some part of the day, which cannot be, otherwise, recorded at that given time.

7.7.4 Classification of Common Cardiac Arrhythmias

Arrhythmia may be classified

- By rate (normal, tachycardia and bradycardia), or
- By mechanism (automaticity, re-entry, fibrillation).

It is also appropriate to classify by site of origin:

1. Atrial

1. Atrial Premature Contractions (APCs)
2. Wandering Atrial Pacemaker
3. Multifocal Atrial tachycardia (MAT)
4. Atrial Flutter (AF)
5. Atrial fibrillation (Afib or Af)

2. Junctional Arrhythmias

1. Supraventricular tachycardia (SVT)
2. AV nodal re-entrant tachycardia is the commonest cause of Paroxysmal Supra-Ventricular Tachycardia (PSVT)
3. Junctional rhythm
4. Junctional tachycardia
5. Premature junctional complex

3. Atrio-ventricular

1. AV re-entrant tachycardia occurs when a re-entry circuit crosses between the atria and ventricles somewhere other than the AV node:
   - A Wolff–Parkinson–White (WPW) syndrome
   - B Lown–Ganong–Levine (LGL) syndrome

4. Ventricular

1. Ventricular Premature Contractions (VPC), sometimes called Ventricular Extra Beats (VEBs)
   - A Premature ventricular beats occurring after every normal beat are termed ventricular bigeminy, i.e., two beats followed by a pause.
   - B Two premature ventricular beats for each normal beat is termed ventricular trigeminy, i.e., three beats and a pause.
2. Accelerated idioventricular rhythm
3. Monomorphic ventricular tachycardia
4. Polymorphic ventricular tachycardia
5. Ventricular fibrillation

5. Heart Blocks

These are also known as AV blocks, because the vast majority of them arise from pathology at the atrioventricular node. They are the commonest cause of bradycardia, next to sinus bradycardia:

1. First-degree heart block, which manifests as PR-prolongation
2. Second-degree heart block
   - A Type 1 second-degree heart block, also known as Mobitz I or Wenckebach's phenomenon
   - B Type 2 second-degree heart block, also known as Mobitz II
3. Third-degree heart block, also known as Complete Heart Block (CHB).

7.8 CARDIAC OUTPUT

Cardiac Output (CO) is the volume of blood pumped by the heart per minute. It is expressed as mL of blood per minute.

Cardiac output is the most important factor in cardiovascular system because the quantity and the rate of blood flow through different parts of the body depends upon the cardiac output.

Cardiac output in mL/min = heart rate (beats/min) X stroke volume (ml/beat)

The heart rate is simply the number of heartbeats per minute.

The stroke volume is the volume of blood, in milliliters (mL), pumped out of the heart with each beat.

Increasing either heart rate or stroke volume increases cardiac output.

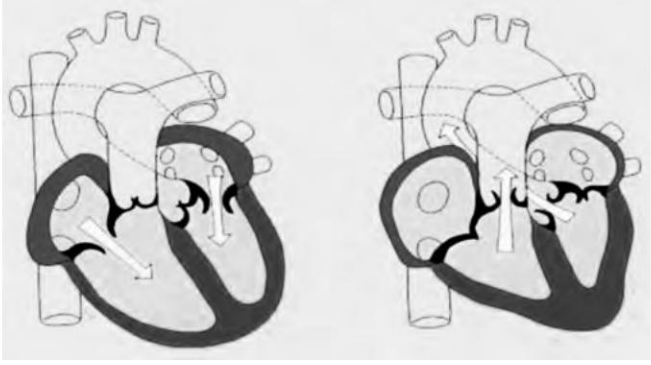


Fig. 7.24 *Heart as a pump*

An average person has a resting heart rate of 70 beats/minute and a resting stroke volume of 70 mL/beat. The cardiac output at rest is

Cardiac output = 70 (beats/min) × 70 (mL/beat) = 4900 mL/minute.

The total volume of blood in the circulatory system of an average person is about 5 liters (5000 mL). The entire volume of blood within the circulatory system is pumped by the heart each minute (at rest). During vigorous exercise, the cardiac output can increase up to 7 fold (35 liters/minute). This increase during exercise is called cardiac reserve. (See Fig. 7.25)

7.8.1 Maintenance of Cardiac Output

1. Control of Heart Rate

The SA node of the heart, called pacemaker, is innervated by both the sympathetic and parasympathetic nerve fibers. The parasympathetic fibers release acetylcholine, which acts to slow the pacemaker potential of the SA node and thus reduces heart rate. Under conditions of physical or emotional activity,

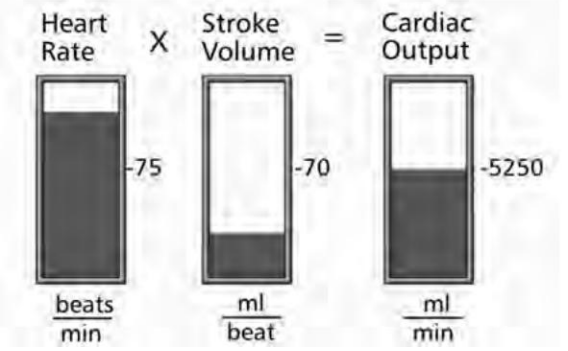


Fig. 7.25 *A sudden drop in blood pressure (e.g., when getting out of bed) results in low venous return and therefore decreased stroke volume. However, heart rate increases due ro sympathetic activity and normal cardiac output is maintained.*

sympathetic nerve fibers release nor epinephrine (noradrenaline), which acts to speed up the pacemaker potential of the SA node, thus increasing heart rate. Sympathetic-nervous-system activity also causes the release of epinephrine (adrenaline) from the adrenal medulla. Epinephrine enters the bloodstream, and is delivered to the heart where it binds with SA node receptors. Binding of epinephrine leads to further increase in the heart rate.

2. Control of Stroke Volume

Under resting conditions, the heart does not fill to its maximum capacity. If the heart were to fill more per beat then it could pump out more blood per beat, thus increasing stroke volume. Also, the ventricles of the heart empty only about 50% of their volume during systole. If the heart were to contract more strongly then the heart could pump out more blood per beat. A stronger contraction would lead to a larger stroke volume. During periods of exercise, the stroke volume increases because of both these mechanisms (the heart fills up with more blood and the heart contracts more strongly).

Stroke volume is increased by 2 mechanisms:

- Increase in end-diastolic volume
- Increase in sympathetic system activity

(a) End-diastolic Volume The stroke volume is determined by the volume of blood in the ventricles immediately before they contract. This is called Ventricular End Diastolic Volume (VEDV). It is also known as **preload**. This depends on the amount of blood returning to the heart through the superior vena cava and inferior vena cava. This is called the **venous return**. An increase in venous return of blood to the heart will result in greater filling of the ventricles during diastole and thus the end-diastolic volume will be increased. The heart will pump out whatever volume is delivered to it. If the end-diastolic volume doubles then stroke volume will double. This is called **Starling's law** which states that the contractile force of the heart is directly proportional to the degree of stretch of myocardial fibers.

(b) Increased Sympathetic Activity The cardiac muscle cells of the ventricular myocardium are richly innervated by sympathetic nerve fibers. Release of norepinephrine by these fibers causes an increase in the strength of myocardial contraction, thus increasing the stroke volume.

(c) Minute Volume Minute volume is defined as the amount of blood pumped out by each ventricle in one minute, i.e., minute volume is equal to the cardiac output.

(d) Cardiac Index The minute volume from ventricles expressed in relation to square meters of body surface is called cardiac index. Thus, cardiac index is defined as the amount of blood pumped out of ventricle per minute per square meter of the body surface area.

7.8.2 Measurement of Cardiac Output

There are a number of clinical methods for measurement of cardiac output, ranging from direct intracardiac catheterization to non-invasive measurement of the arterial pulse.

The different methods are

1. Fick principle
2. Dilution methods
3. Pulmonary artery thermodilution (trans-right-heart thermo dilution)
4. Doppler ultrasound method
5. Pulse pressure methods

7.8.3 Variations in Cardiac Output

Cardiac output can increase or decrease in certain situations. There are two categories:

1. Physiological
2. Pathological

1. Physiological Variations

1. CO is more in children than in adults.
2. CO is more in females than in males.
3. During later months of pregnancy, cardiac output increases considerably.
4. Depending on the severity of exercise, cardiac output increases.
5. Cardiac output is less in morning and increases during daytime. This is called **diurnal variation**.
6. With rise in body temperature, e.g., in fever, the cardiac output increases.
7. Emotional conditions like fear, excitement, anxiety, increase cardiac output many-fold. This is due to release of catecholamines which increase heart rate and the force of contraction.

8. The cardiac output increases at higher altitudes. Due to lack of O_2 there is secretion of adrenaline which increases both heart rate and stroke volume.

2. Pathological Variations

Increase in cardiac output is noted when there is hypoxia (as in anemia) or increased need at tissue level of nutrients (as in fever) and due to increased basal metabolism seen in hyperthyroidism.

Decrease in cardiac output is seen in many conditions:

1. Decrease in basal metabolism, as in hypothyroidism, causes decrease in cardiac output.
2. Various cardiac conditions result in decrease in CO:
   - In atrial fibrillation, there is incomplete filling of the heart and hence CO decreases.
   - In heart block, defective pumping action of the heart leads to decrease in CO.
   - Contraction of the heart becomes weak in cardiac failure leading to decrease in CO.
   - Decrease in blood volume seen in dehydration and hemorrhage. Blood loss results in decrease in the blood volume and so there is decrease in venous return and decreased CO.

7.8.4 Distribution of Cardiac Output

The whole amount of blood pumped out by the right ventricle goes to the lungs. The blood pumped by the left ventricle is distributed to different parts of the body.

This distribution of cardiac output is according to the metabolic activities of various regions of the body, e.g., splanchnic (abdominal) circulation is more after meals.

7.8.5 Factors Maintaining Cardiac Output

CO is maintained by certain factors of which venous return is the most important.

1. Venous Return

Venous return is the major determinant of cardiac output.

Venous Return (VR) is the flow of blood back to the heart. Venous return must equal Cardiac Output (CO) Otherwise, blood would accumulate in either the systemic or pulmonary circulations. Although cardiac output and venous return are interdependent, each can be independently regulated.

Venous return is influenced by several factors:

(a) Muscle Contraction Rhythmical contraction of limb muscles as occurs during walking, running, swimming, promotes venous return by the muscle-pump mechanism. In this mechanism, when the muscle contracts, the vein in between is compressed. The valve proximal to the compression opens and blood flows upwards. During relaxation, the proximal valve closes and prevents backflow of blood, and the valve distal to the muscle opens and blood flows upwards. This mechanism goes on and blood flows towards the heart.

(b) Decreased Venous Compliance Sympathetic activation of veins (venoconstriction) decreases venous compliance, increases central venous pressure and promotes venous return indirectly by augmenting cardiac output.

(c) Respiratory Activity or Respiratory Pump During inspiration, intrathoracic pressure decreases and hence the venous return increases, and intra-abdominal pressure increases due to descent of the diaphragm. Flow of blood to right atrium is thus increased.

(d) Vena Cava Compression An increase in the resistance of the vena cava, as occurs when the thoracic vena cava is compressed during a Valsalva maneuver or during the later stages of pregnancy, decreases venous return.

(e) Gravity Gravity helps venous return from head and neck when standing or sitting, while less resistance is offered to venous return from the lower parts of the body when the person lies down.

2. Peripheral Resistance

Peripheral resistance affects the cardiac output because it offers resistance to the blood which is pumped from the ventricles into the great arteries and beyond, i.e., entire arterial tree and its branches. With increase in the resistance, cardiac output decreases, i.e., it is inversely proportional to CO.

3. Blood Volume

When blood volume decreases, venous return decreases and cardiac output decreases.

4. Heart Rate

When heart rate increases markedly, there is decrease in CO due to decrease in diastole and reduced filling.

7.9 BLOOD PRESSURE

Hemodynamic refers to the study of movement of blood through the circulatory system. The major function of cardiovascular system is to pump blood and to circulate it through different parts of the body. It is essential to maintain Blood Pressure (BP) so that the volume of blood supplied to different parts of the body remains adequate. The circulatory system carries out these functions.

Blood pressure is the lateral force or pressure exerted by the column of blood on the walls of blood vessels.

The pressure of the circulating blood decreases as blood moves through arteries, arterioles, capillaries, and veins. The term 'blood pressure' generally refers to arterial pressure, i.e., the pressure in the larger arteries, the blood vessels that take blood away from the heart.

7.9.1 Types of Blood Pressure

Arterial blood pressure is expressed in different terms:

1. Systolic pressure
2. Diastolic pressure
3. Pulse pressure
4. Mean arterial pressure

1. Systolic Pressure

Systolic pressure is the maximum pressure exerted in the arteries during the systole of the heart. It is the peak pressure in the arteries, which occurs at the beginning of the cardiac cycle when the left ventricle contracts and pushes blood into the aorta.

In adults it is about 120 mmHg.

2. Diastolic Pressure

Diastolic pressure is the minimum pressure in the arteries which occurs near the end of the cardiac cycle when the ventricles are resting after the ejection of blood.

In adults it is about 80 mmHg.

3. Pulse Pressure

The difference between systolic and diastolic blood pressures is called pulse pressure.

In adults it is about 40 mmHg.

4. Mean Arterial Pressure

This is the average pressure existing in the arteries. It is not the arithmetic mean of systolic and diastolic pressures. This is the diastolic pressure plus one third of pulse pressure.

To determine mean pressure, diastolic pressure is considered rather than systolic pressure. This is because the diastolic period of cardiac cycle is longer than the systolic period.

7.9.2 Control of Blood Pressure

Blood pressure is controlled in the following ways:

1. Short-term control on a moment-to-moment basis which mainly involves the baroreceptors, chemoreceptors and the higher centers
2. Long-term control involves regulation of blood volume by the kidneys and renin-angiotensin-aldosterone system
3. Hormonal regulation
4. Local regulation

1. Short-term Control

(a) Baroreceptor Reflex The autonomic nervous system is the most rapidly responding regulator of blood pressure. It receives continuous information from the baroreceptors (pressure-sensitive nerve endings) situated in the carotid sinus and the aortic arch. This information is relayed to the brainstem to the VasoMotorCenter (VMC). The VMC is a collection of interconnected neurons in the brain and is situated within the medulla and the pons. A decrease in blood pressure causes activation of the sympathetic nervous system, resulting in increased contractility of the heart (beta receptors) and vasoconstriction of both the arterial and venous side of the circulation (alpha receptors). This leads to increase in BP. Conversely, it is true for increase in BP.

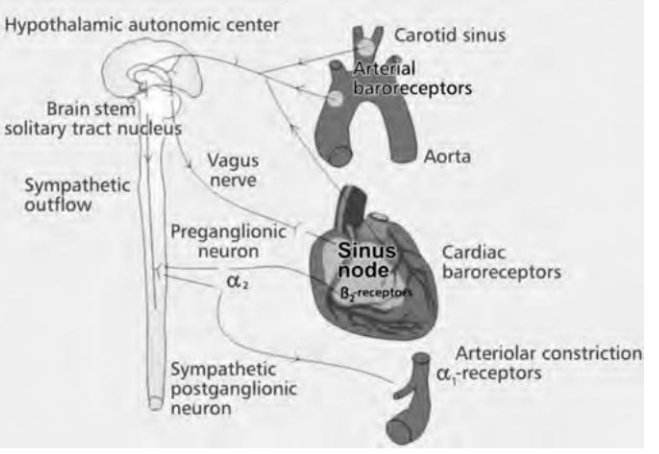


Fig. 7.26 *Autonomic cardiovascular control*

The baroreceptor control of blood pressure is also called baroreceptor reflex.

(b) Chemoreceptors These are nerve endings situated in the carotid and aortic bodies. Primarily, they are involved in

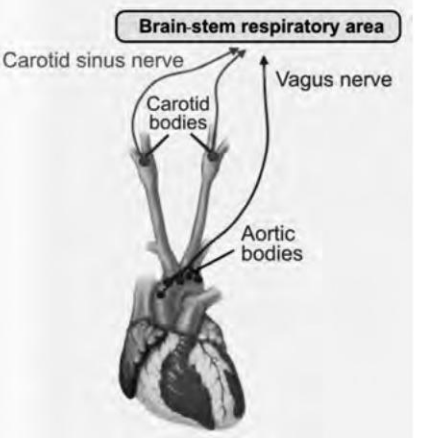


Fig. 7.27 *Chemoregulation of blood pressure*

the control of respiration as they are sensitive to changes in the levels of carbon dioxide, oxygen and the acidity of blood.

They come in action only when severe disruption of respiratory function occurs or when arterial BP falls to less than 80 mmHg.

Increase in the acidity of blood, increase in PCO_2 and decrease in PO_2, stimulate the chemoreceptors, which in turn act on the VMC and there is increase in heart rate and stroke volume which increases the blood pressure.

Decrease in PO_2 leads to vasoconstriction and this also increases the blood pressure. Decrease in the acidity of blood, decrease in PCO_2 and increase in PO_2, acts on the chemoreceptors and there is effect on the VMC, which leads to decrease in stroke volume and in heart rate. This causes decrease in blood pressure.

Increase in PO_2 causes vasodilatation and this also decreases the blood pressure.

(c) Higher Centers in the Brain Emotional states like fear, anxiety, pain and anger influence higher centres and they stimulate the VMC and lead to rise of blood pressure.

The hypothalamus in the brain controls body temperature and influences VMC which responds by adjusting the diameter of blood vessels in the skin; this is an important mechanism in adjusting heat loss and retention of fluids and thereby control of blood pressure.

2. *Long-term Control*

The kidneys help regulate blood pressure by increasing or decreasing the blood volume and also by the renin–angiotensin system. They are the most important organs for the long-term control of blood pressure.

(a) Regulation of Extracellular Fluid Volume When extracellular fluid volume increases, blood volume increases and this causes increase in arterial blood pressure. Kidneys excrete more amounts of water and salt, especially sodium. The extracellular fluid volume decreases and thus, the arterial blood pressure is reduced.

When blood pressure decreases due to decreased extracellular fluid volume, there is increased reabsorption of water from renal tubules and extracellular fluid volume is restored, and thereby the blood pressure increases.

(b) Renin–Angiotensin Mechanism

Renin and angiotensin production is increased in the kidney when stimulated by hypotension, reduced renal blood flow or fall in sodium level. Renin is released into the blood and acts on a plasma protein called angiotensinogen and converts it into Angiotensin I, which is converted in the lung (by angiotensin-converting enzyme) to Angiotensin II, a potent vasoconstrictor.

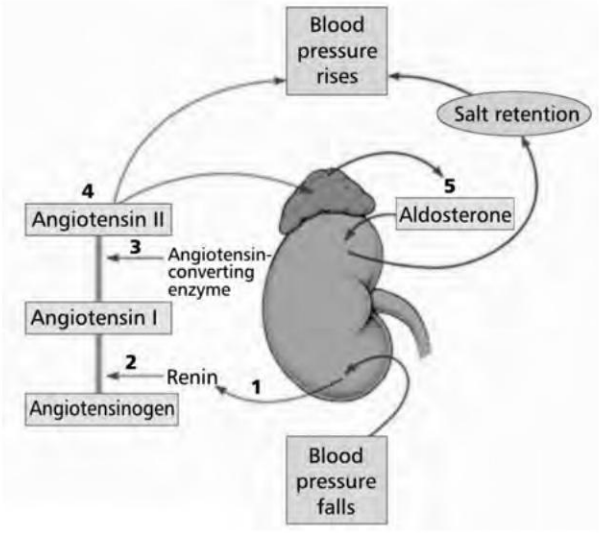


Fig. 7.28 *Renin–angiotensin mechanism*

1. Angiotensin II causes constriction of arterioles which results in increase in peripheral resistance leading to increase in blood pressure.
2. Simultaneously, it also causes constriction of afferent arterioles in kidney. This leads to retention of water and salts. Hence there is increase in extracellular fluid volume. This restores the blood pressure to normal.
3. In addition, these hormones stimulate the production of aldosterone from the adrenal cortex which decreases urinary fluid and electrolyte loss from the body and increases reabsorption of sodium from renal tubules. Sodium reabsorption is followed by water reabsorption. The extracellular fluid volume increases. The blood pressure thus becomes normal.

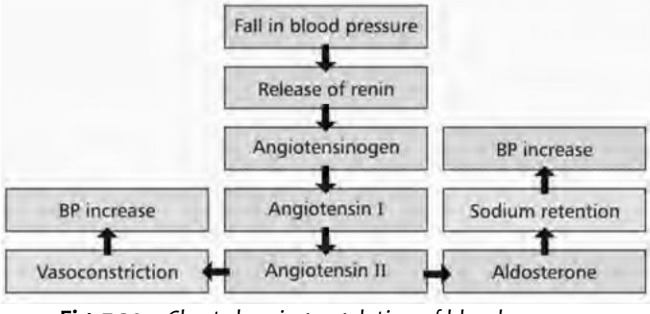


Fig. 7.29 *Chart showing regulation of blood pressure*

This system is responsible for the long-term maintenance of blood pressure but is also activated very rapidly in the presence of hypotension.

3. *Hormonal Regulation*

Hormonal mechanism exists both for lowering and raising blood pressure. They act in various ways, including vasocon-

striction, vasodilatation and alteration of blood volume. The principal hormones affecting blood pressure are adrenaline and noradrenaline. They are secreted by the adrenal medulla in response to sympathetic nervous system stimulation. They increase cardiac output and cause vasoconstriction and act very rapidly.

- Thyroxine increases systolic blood pressure and decreases diastolic blood pressure.
- Angiotensin and serotonin increase blood pressure by vasoconstriction.
- Bradykinin decreases blood pressure by vasodilatation.
- Acetylcholine also decreases blood pressure by vasodilatation.

4. Local Regulation of Blood Pressure

Local Control in the Capillary Beds Nitric oxide (NO) is a potent dilator of arteries and arterioles. When the endothelial cells lining these vessels are stimulated, they synthesize nitric oxide. It quickly diffuses into the muscular walls of the vessels causing them to relax. In addition, as the hemoglobin in red blood cells releases its O_2 in tissues, the lowered pH causes it to release NO, which further helps to dilate the vessels to meet the increased need of the tissue.

There are some local substances which can alter the blood pressure by vasoconstriction or vasodilatation.

Local vasoconstrictors increase blood pressure, e.g., endothilins of endothelial origin. They produce this effect by stretching of the blood vessels.

Local vasodilatators are of two types and they decrease the blood pressure. They are either of metabolic origin or of endothelial origin.

7.9.3 Measurement of Blood Pressure

The **direct method** is employed only in animals.

The indirect method can be carried out by an apparatus called **sphygmomanometer**.

It is carried out by

1. Palpatory method by palpating the brachial pulsations
2. Auscultatory method by the use of a stethoscope
3. Oscillometric method by an apparatus

Blood-pressure measurements can be taken in the clinic, at home, and by ambulatory blood-pressure monitoring. A mercury sphygmomanometer is used in most of the clinics. Aneroid and automated sphygmomanometers have gained popularity over recent years. Before measuring, patients should be seated for at least 5 minutes or made to lie down in quiet surroundings. Cuffs of the appropriate size should be used. The center of the cuff should be at heart level and applied on the front of the arm about 3 cm above the elbow. Then air is inflated into the cuff normally above the expected systolic pressure and then slowly released. The stethoscope is placed on the brachial artery at the elbow and sounds are heard.

Fig. 7.30 *Instruments to measure blood pressure*

The onset of sounds (tapping sounds) corresponds to systolic pressure. The disappearance of sound corresponds to the diastolic pressure. It is important to pay attention to cuff placement, stethoscope placement, and the rate of deflation of the cuff. Blood pressure should be measured in both the arms on the first visit.

The fully automated, oscillometric technique is not routinely used in clinical practice and is generally reserved for patients who are not ambulatory.

7.9.4 Variations in Blood Pressure

1. Physiological
2. Pathological

Physiological Variations

1. Arterial blood pressure usually increases as age advances.
2. The arterial pressure is low in females as compared to males of the same age up to menopause; after menopause, it becomes equal.
3. Pressure is more in obese persons as compared to lean persons.
4. When a person is resting, pressure decreases. Pressure is reduced during sleep.
5. Blood pressure increases for a few hours after meals due to increase in cardiac output.
6. Blood pressure is slightly low early in the morning; it gradually rises at noon and becomes low in the evening. This is called diurnal variation.
7. During anxiety, fear or excitement, blood pressure increases due to release of adrenaline.
8. After exercise, systolic blood pressure should rise, whereas diastolic blood pressure usually remains approximately the same or drops. After severe exercise, the diastolic pressure drops due to decrease in peripheral resistance (during exercise, metabolic end products accumulate in the skeletal muscles which produce vasodi-

latation and results in decrease in peripheral resistance). If there is hypotension after moderate exercise, it may predict coronary artery disease.

Pathological Variations

1. Hypertension
2. Hypotension

7.10 CIRCULATION

The circulatory system is a biological organ system whose primary function is to move substances to and from the cells, via the medium of blood and blood vessels.

It moves nutrients, gases, and wastes to and from cells for growth, repair, to help fight diseases, to help stabilize body temperature and pH and to maintain homeostasis.

The main components of the human circulatory system are the heart, the blood, and the blood vessels.

When the heart contracts, it pushes the blood out into two major loops or cycles. In the systemic loop, the blood circulates into the body's systems, bringing oxygen to all its organs, structures and tissues and collecting carbon dioxide waste. In the pulmonary loop, the blood circulates to and from the lungs to release the carbon dioxide and pick up oxygen. The systemic cycle is controlled by the left side of the heart and the pulmonary cycle by the right side of the heart.

The overall blood circulatory system is made up of four subsystems.

1. Arterial Circulation

Arterial circulation is that part of the blood circulatory system that involves arteries and its branches like the aorta and pulmonary arteries and their branches.

2. Venous Circulation

Venous circulation is the part of blood circulatory system that involves veins like the vena cavae and pulmonary veins. Veins are blood vessels that carry blood to the heart.

3. Capillary Circulation

Capillary circulation is the part of the circulatory system where oxygen, nutrients, and waste pass between blood and parts of the body.

4. Pulmonary Circulation

Pulmonary circulation is the movement of blood from the heart to the lungs and back to the heart again. It includes both arterial and venous circulation. It is described below in details.

7.10.1 Circulation through Special Regions

There are other circulations which are also included. They are circulation through special regions, viz., coronary circulation, lymphatic circulation, portal circulation, cerebral circulation, splanchnic circulation and placental-fetal circulation.

Coronary Circulation

The heart itself needs to be supplied with blood. This is delivered by the two coronary arteries and their branches.

The vessels that deliver oxygen-rich blood to the myocardium are known as **coronary arteries**. The vessels that remove the deoxygenated blood from the heart muscle are known as **coronary veins**.

The coronary arteries receive 4 % of the total blood pumped from the heart, even though the heart comprises a small proportion of the body weight. This highlights the importance of the heart as regards the body functions.

The **right coronary artery** takes its origin from the aorta just distal to the aortic valve and appears on the surface of the heart between the pulmonary trunk and the auricle of the right atrium. Major branches of the right coronary artery include its marginal branch, posterior interventricular branch, and AV nodal branch. The right coronary artery supplies blood to the right atrium, right ventricle, and variable portions of the left atrium and left ventricle. In 50 to 60 % of persons, the right coronary artery is larger and supplies more blood to the heart than the left coronary artery.

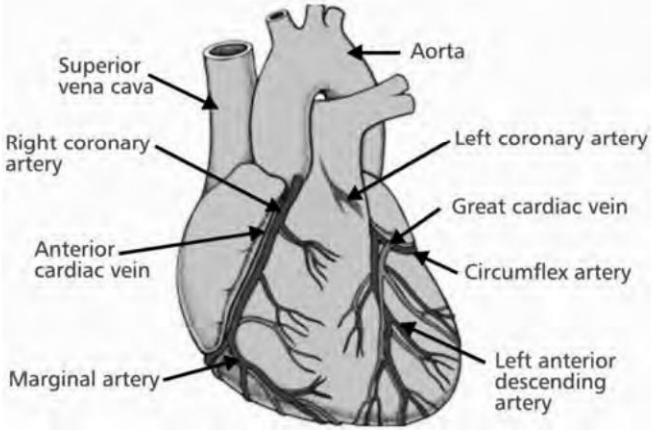


Fig. 7.31 *Coronary circulation*

The **left coronary artery** also arises from the base or ascending portion of the aorta. It is at first located between the pulmonary trunk and auricle of the left atrium. Major branches of the left coronary artery include its anterior interventricular branch and its circumflex branch. The left coronary artery supplies ventricles, the inter-ventricular septum and the left atrium.

The coronary arteries divide and subdivide into smaller branches which run all along the surface of the heart.

Smaller branches are called **epicardial arteries**. They give rise to further smaller branches known as **final arteries** or **intramural vessels**.

The final arteries run at right angles to the heart muscle near the inner aspect of the wall of the heart.

The coronary arteries are classified as 'end circulation', since they represent the only source of blood supply to the myocardium.

7.10.2 Coronary Blood Flow (CBF) and Its Measurement

The heart receives (at rest) about 4% of the cardiac output, or 250 mL/min. CBF is governed by a pressure gradient generated between cardiac chambers and the aorta and by resistance of the vessels.

Various methods are suggested for measurement of coronary blood flow:

1. Clearance methods
2. Thermodilution
3. Flow-meter techniques
4. Catheter-tip flowmeters

Coronary blood flow can be measured directly by using a flow meter. An electromagnetic flow meter is directly placed around any coronary artery and the necessary information is obtained. This is the most commonly used technique.

Phasic Changes in the Coronary Blood Flow

Blood flow through coronary arteries is not constant. During contraction of the ventricular myocardium (systole), the subendocardial coronary vessels are compressed due to the high intraventricular pressures. However, the epicardial coronary vessels remain patent. Because of this, blood flow in the sub-endocardium stops. As a result, most myocardial perfusion occurs during heart's relaxation (diastole) when the sub-endocardial coronary vessels are patent and under low pressure.

Aortic pressure plays an important role in the phasic changes of coronary blood flow.

Factors Regulating Coronary Blood Flow

Like any other organ, the heart by auto-regulation mechanism, has the capacity to regulate its own blood flow. Various factors are involved in the auto-regulation mechanism.

Regulation of blood flow occurs through local intrinsic regulation, mostly through production of vasodilating metabolites in response to minimal degrees of ischemia. Local regulation dominates over remote regulation in most circumstances.

Factors regulating coronary blood flow are the following:

(a) Need for Oxygen Exercise is the most important physiological stimulus for increased myocardial oxygen demand.

(b) Metabolic Factors Whenever the oxygen consumption becomes higher, various substances promote regional vasodilatation reducing the resistance, thereby increasing CBF. Among these vasoactive metabolic substances are adenosine, potassium, lactate and prostaglandins.

(c) Coronary Perfusion Pressure The total pressure in the aorta is a sum of two components: the dynamic pressure plus the lateral pressure. The sum of these two parameters must be constant. The dynamic pressure is proportional to the blood velocity, while the lateral component is actually the driving force for perfusing the coronary arteries.

7.11 VENOUS DRAINAGE—HEART

Blood drains into the following vessels.

(a) Coronary Sinus Most of the blood supplied by the coronary arteries is returned to the right atrium by way of the coronary sinus. It drains 75% of total coronary blood flow.

(b) Anterior Coronary Veins They drain blood from the right side of the heart and open into the right atrium.

(c) Other Veins Numerous microscopic veins, the **venae cordis minimae**, open directly into the heart chamber. They drain blood from myocardium directly into the concerned chamber of the heart.

7.11.1 Applied Physiology

The most common cause of myocardial ischemia is coronary atherosclerosis, which produces progressive stenosis, reducing CBF. The atheroma plaque—deposition of cholesterol—causes partial obstruction of the lumen. The perfusion pressure will be lower at the point distal to the obstruction; myocardial infarct is much more likely to occur if the heart cannot have another way to supply blood to the suffering myocardium. Clinically, coronary artery disease is manifested by angina pectoris in a great majority of people. The pain is usually triggered when oxygen demand increases, as in exercise (effort angina). This pain starts below the sternum or over the chest and may radiate to the left arm and the left shoulder.

In this situation, the coronary blood flow will try to increase but the narrowed segment will offer a great resistance and

regional ischemia will develop, if compensatory mechanisms fail. If the quantum of myocardium affected by ischemia is less, then blood flow can be restored by rapid development of coronary collateral circulation.

If the obstruction is severe or if a clot develops in the artery blocking it totally, ischemia leads to necrosis and death of that part of the myocardium. This is called **myocardial infarction**.

7.11.2 Types of Circulation

1. Pulmonary Circulation

Pulmonary circulation is the portion of the cardiovascular system which carries deoxygenated blood away from the heart, to

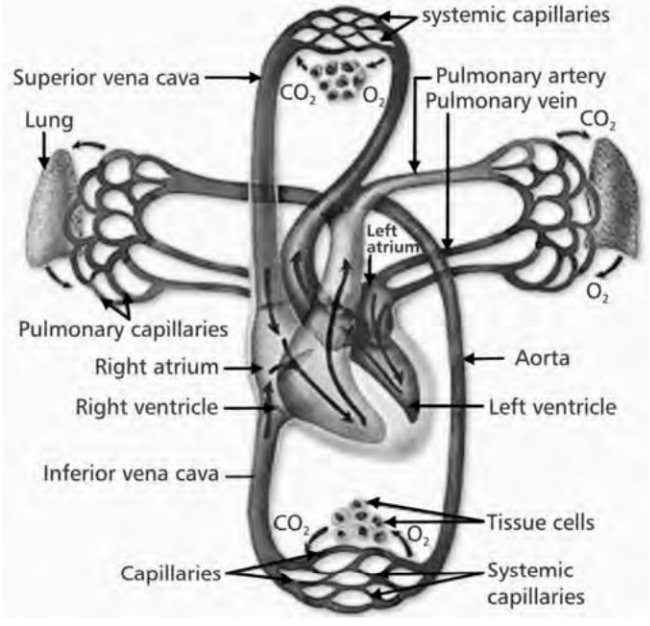


Fig. 7.32 *Pulmonary circulation (Refer colour figure)*

the lungs, and returns oxygenated blood back to the heart.

Deoxygenated blood from the body leaves the systemic circulation and enters the right heart (right atrium) through the superior vena cava and the inferior vena cava. The blood is then pumped through the tricuspid valve into the right ventricle. The pulmonary artery leaves the right ventricle and divides into two arteries, one for each lung. In the lungs, it divides into two branches. Within the lungs they divide and subdivide into arterioles and capillaries. In the capillaries of the alveoli, red blood cells release carbon dioxide and pick up oxygen during respiration.

The oxygenated blood then leaves the lungs through pulmonary veins, which return it to the left heart, completing the pulmonary cycle. This blood then enters the left atrium, which pumps it through the bicuspid valve into the left ventricle. The blood is then distributed to the body through the systemic circulation before returning again to the pulmonary circulation.

2. Portal Circulation

The gastric, splenic and mesenteric veins, which collect the venous blood from all the digestive organs, unite to form the portal vein. The blood which has circulated through the capillaries of the stomach, pancreas and the intestine reaches the liver via the portal vein. It contains the products of digestion. This vein breaks up into capillaries and distributes this blood throughout the liver. There it mingles with the blood supplied by the hepatic artery, and is collected again by small veins which unite to form the hepatic vein, by which it is carried to the inferior vena cava which pours it into the right atrium.

3. Cerebral Circulation

Cerebral circulation is the movement of blood through the network of blood vessels supplying the brain. The arteries deliver oxygenated blood, glucose and other nutrients to the brain and the veins carry deoxygenated blood back to the right side of the heart from where it is sent to the lung for removal of carbon dioxide, lactic acid, and other metabolic products. The amount of blood that the cerebral circulation carries is known as **cerebral blood flow**.

There are two main pairs of arteries that supply the cerebral arteries.

Carotid arteries and their branches (referred to as the anterior circulation) supply the anterior portion of the brain while the **vertebrobasilar system** (referred to as posterior circulation) supplies the posterior portion of the brain.

Venous blood flows peripherally via superficial cerebral veins and centrally via the deep cerebral veins into the venous sinuses (lying between the outer endosteal and the inner meningeal layer of the dura) which drain into the internal jugular vein.

4. Splanchnic Circulation

The circulation of blood through the vessels supplying the abdominal viscera is called splanchnic circulation. It is further divided into mesenteric circulation, splenic circulation and hepatic circulation.

5. Placental and Fetal Circulation

Throughout the fetal stage of development, the maternal blood supplies O_2 and nutrients to the fetus and carries away its wastes. These substances diffuse between the maternal and fetal blood through the placental membrane. They are carried to and from the fetal body by the umbilical blood vessels.

In the fetal circulatory system, the umbilical vein transports blood rich in O_2 and nutrients from the placenta to the fetal body. After birth when the umbilical cord is cut, no more blood flows through the umbilical arteries and the vein and they

degenerate. The initial inflation of the lungs causes important changes in the circulatory system.

6. Lymphatic Circulation

The lymphatic system has neither a heart nor arteries. Its microscopic dead-end capillaries extend into most tissues, paralleling the blood capillaries. The lymphatic circulation is a drainage system. It collects excess interstitial fluid and returns it to the blood. It also returns plasma proteins to the blood. Once interstitial fluid enters a lymph capillary, it is referred to as lymph.

The three main types of lymphatic vessels are lymph capillaries, lymphatics, and lymph ducts. Lymph capillaries are microscopic tubes located between cells. They somewhat resemble blood capillaries, but differ in important ways. Whereas a blood capillary has an arterial and a venous end, a lymph capillary has no arterial end. Instead, each lymph capillary originates as a closed tube. Lymph capillaries also have a larger and more irregular lumen (inner space) than blood capillaries and are more permeable.

7.12 INVESTIGATIONS IN CARDIOLOGY

1. ECG

It has been discussed with the physiology of the system.

2. Holter Monitoring

It is a specialized ECG test which is a continuous recording of ECG for 24–48 hours. It is useful for evaluating intermittent arrhythmias.

3. Exercise Tolerance Test (Treadmill Test) TMT

Exercise tolerance testing is an important diagnostic and prognostic tool for assessing patients with suspected or known ischemic heart disease. During exercise, coronary blood flow must increase to meet the higher metabolic demands of the myocardium. Limiting the coronary blood flow may result in electrocardiographic changes.

Exercise tolerance testing (also known as exercise testing or exercise stress testing) is used routinely in evaluating patients who present with chest pain, in patients who have chest pain on exertion, and in patients with known ischemic heart disease.

7.12.1 Non-invasive Cardiac Imaging

1. Echocardiography

Cardiovascular imaging has significantly enhanced the practice of cardiology over the past few decades.

Two-dimensional (2D) echocardiography is able to visualize the heart directly in real time using ultrasound, providing instantaneous assessment of the myocardium, cardiac chambers, valves, pericardium, and great vessels.

3D echocardiography is another advanced modality in echocardiography studies.

2. Transesophageal Echocardiography (TEE)

TEE provides a unique window for high-resolution imaging of posterior structures of the heart, particularly the left atrium, mitral valve and aorta.

3. Stress Echocardiography

2D and Doppler echocardiography are usually performed with the patient in the resting state. Further information can be obtained by re-imaging during either exercise or pharmacologic stress. The primary indications for stress echocardiography are to confirm the suspicion of ischemic heart disease and estimate its severity.

4. Doppler Echocardiography

Doppler echocardiography measures the velocity of moving red blood cells and has become a non-invasive alternative to cardiac catheterization for assessment of hemodynamic.

5. Color-flow Doppler Imaging

Color-flow doppler imaging displays the blood velocities in real time superimposed upon a 2D echocardiographic image. The different colors indicate the direction of blood flow (red toward and blue away from the transducer).

7.12.2 Nuclear Cardiology and MRI/CT Imaging

Nuclear cardiology uses isotopes to assess myocardial perfusion and ventricular function and has contributed greatly to the evaluation of patients with ischemic heart disease.

Basic Principles of Nuclear Cardiology

All nuclear cardiology studies depend on the injection into the patient of an isotope that emits photons, generally gamma rays, generated during radioactive decay when the nucleus of an isotope changes from one energy level to a lower one. Radionuclide imaging uses a special camera that images these photons.

Cardiac MRI and CT can delineate cardiac structure and function with high resolution. They are particularly useful in the examination of cardiac masses, the pericardium and the great vessels.

MRI stress testing now makes possible examination of both ventricular function and perfusion. Detection of coronary calcification by CT as well as direct visualization of coronary arteries by CT Angiography (CTA) is of growing utility in patients with suspected Coronary Artery Disease (CAD).

Gated Single-Photon Emission Computed Tomography (SPECT) is the nuclear cardiology technique that is most commonly utilized to assess ejection fraction and regional-wall motion abnormality.

(a) Single-Photon Emission Computed Tomography (SPECT) In single-photon emission computed tomography, thallium is used to study the perfusion and the integrity of cell membrane.

(b) Positron Emission Tomography (PET) The gamma emission is detected by the gamma camera in the PET scanner. PET cameras are considerably more expensive than conventional nuclear cardiology cameras. Rubidium-82 is the most commonly used positron emitter.

(c) Magnetic Resonance Imaging (MRI) MRI is a technique based on the magnetic properties of hydrogen nuclei. They release energy in the form of electromagnetic radiation that is detected and processed into an image. Contrast agents, such as gadolinium, are frequently employed to produce magnetic resonance angiograms.

(d) Computed Tomographic Imaging CT is fast, simple, non-invasive, and provides images with excellent spatial resolution and good soft-tissue contrast.

(e) Contrast-Enhanced CT Angiography With the high temporal and spatial resolution of multislice spiral CT, accurate assessment of luminal narrowing in the major branches of the coronary arteries is possible in selected patients. It can be performed in a patient suspected with ischemia who cannot be subjected to a stress test.

7.12.3 Cardiac Procedures (Invasive)

Normally, the inner wall of the artery is smooth and blood flows with minimum interference. As years go by, in a significant number of people, coronary arteries get affected by atherosclerosis, and thereby the inner lining of the arteries get thickened and rough because of fatty (cholesterol) deposits. The passage gets narrowed, producing stenosis leading to block. Because of less blood supply to the heart, a person develops chest pain on exertion. This is called **angina**.

When angina is not controlled by medication, coronary angiography is suggested. It is a gold-standard investigation which is the only absolute way to evaluate coronary artery disease. It is usually performed as part of cardiac catheterization which includes LV angiography and hemodynamic measurements.

1. Cardiac Catheterization

A catheter is a thin radiopaque tube, made up of elastic material (rubber, plastic, glass or metal). The insertion of a catheter into a blood vessel or heart is called cardiac catheterization. The procedure can be safely performed as a day-care procedure.

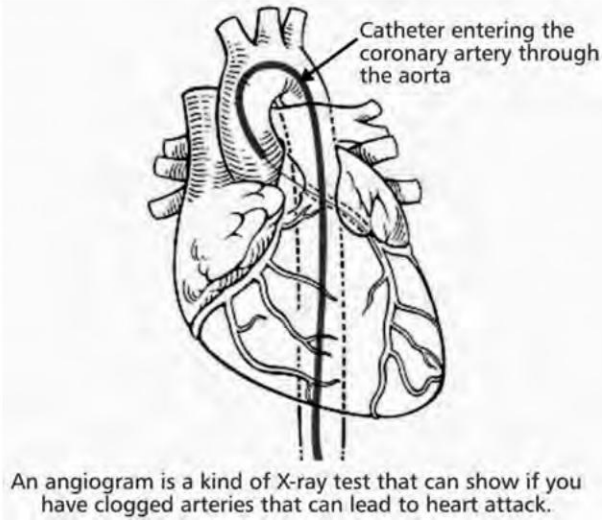


Fig. 7.33 *Catheter in coronary artery*

It has both diagnostic and therapeutic value. It gives valuable information regarding the need for cardiac surgery, coronary angioplasty and other therapeutic procedures.

Under local anesthesia, a catheter is introduced via the femoral, brachial or radial route into the arteries. The catheter is introduced up to the opening of the coronary artery. Contrast medium is injected and multiple X-ray images are obtained from various angles and recorded. This helps in detecting the blocks and helps in deciding whether balloon angioplasty or Coronary Artery Bypass Graft Surgery (CABG) is necessary for management.

Complications These are very rare and include

1. Bleeding and edema (swelling) at the local site
2. Coronary artery dissection
3. Stroke
4. Death

2. Angioplasty

Angioplasty is a medical procedure—an intervention in which a balloon is used to open the narrowed or blocked blood vessel of the heart.

The catheter is introduced, as in coronary angiography, and

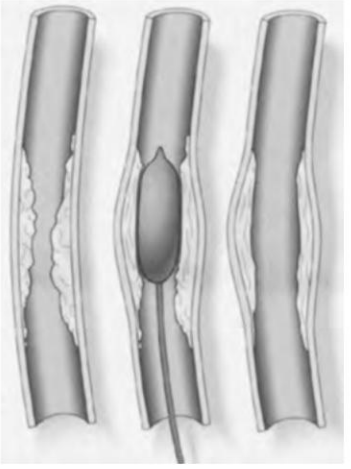


Fig. 7.34 *Balloon angioplasty*

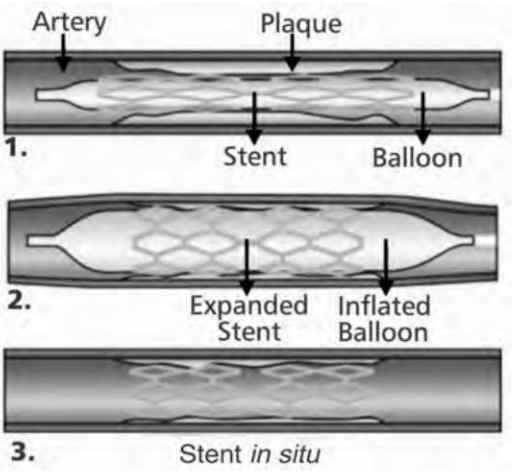


Fig. 7.35 *Stent with balloon angioplasty*

then the balloon catheter is inserted up to the blocked coronary artery and then inflated, thus indenting or opening the blocked vessel, which restores the blood flow to the heart muscle.

In almost all cases, a device called stent is also placed at the site of narrowing or blockage in order to keep the artery open, i.e., to prevent restenosis.

A stent is a wire mesh tube used to keep the artery (that is recently been cleared using balloon angioplasty) open.

When the balloon is inflated, the stent expands, locks in space, and forms a scaffold. This holds the artery open. The stent stays in the artery permanently, and holds the artery patent. This improves blood flow to the heart muscle.

In recent years, new types of stents, called Drug Eluted Stents (DES) are being used, instead of plain stents. These are coated with drug, which is slowly released, which in turn prevents thrombus formation at or around the stent. This prevents reclosing of blood vessels.

A very small percentage of patients need an emergency Coronary Artery Bypass Graft (CABG) surgery when angioplasty fails to open the artery.

3. Coronary Artery Bypass Graft (CABG) Surgery

Bypass surgery is a procedure in which a healthy blood vessel (artery or vein obtained from the patient) is used to form bypass around a blockage in a coronary artery. The new blood

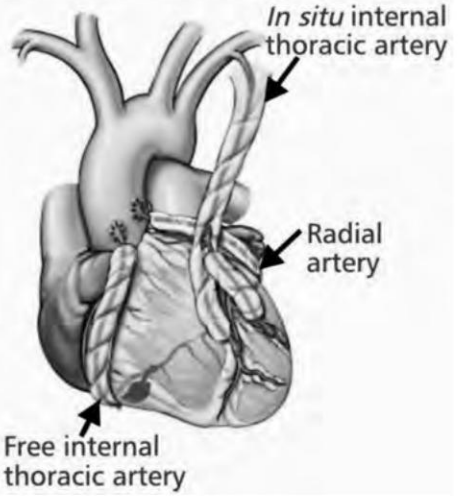


Fig. 7.36 *Radial artery graft*

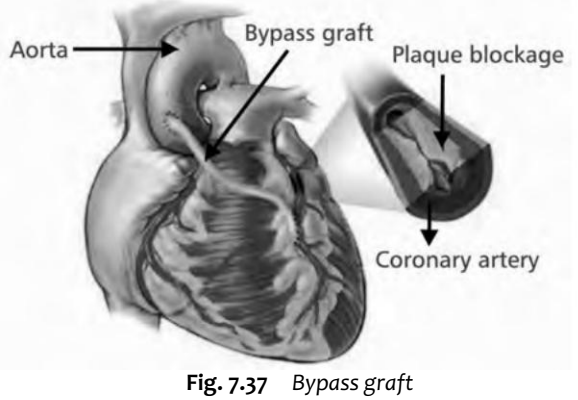


Fig. 7.37 *Bypass graft*

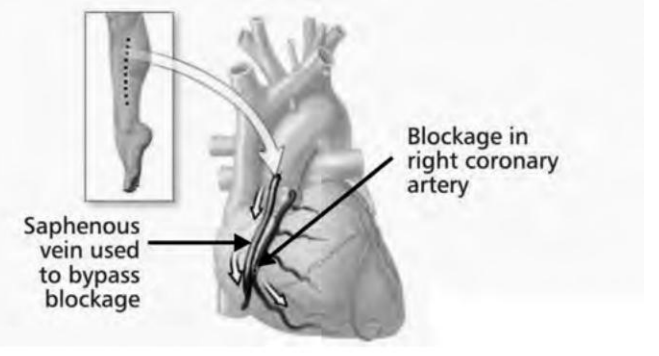


Fig. 7.38 *Venous graft*

vessel used is called graft; and hence the procedure is termed Coronary Artery Bypass Graft Surgery—CABG. One end of the graft is sewn to the aorta proximal to the stenosed segment and the other end is sewn to the coronary artery/aorta distal to the blockage.

The original blockage in the artery remains as it is but now there is adequate blood supply to the heart muscle beyond the blockage through the bypass route. Today, CABG is one of the most frequently performed surgical procedures.

The graft used can be either an artery or a vein. Most advanced heart centers prefer to use arterial grafts, since they have been shown to have a longer life. One, two or three grafts are done depending upon the blocks in three main vessels of the heart.

4. Beating Heart Surgery

To perform CABG surgery, the surgeons always use a heart–lung machine. This machine allows the heart to be stopped for a while to perform the grafting.

However, in the past few years, some of the surgeons also perform the surgery on a beating heart. They do not use the heart–lung machine which has its own drawbacks.

Here, a device called **octopus** is used and the surgery is done while the heart is beating. This method has several advantages.

1. The patient spends less time in ICU.
2. Less blood transfusion is needed and hence blood-transfusion-related complications are less.
3. The patient has a shorter hospital stay.

The disadvantage is that it is technically more demanding.

Very recently, more modern techniques are coming up but are in the experimental stage.

To improve myocardial blood supply in patients with ungraftable vessels, the techniques of Trans Myocardial Laser Revascularization (TMLR) and angiogenesis have provided new options. The application of robot-assisted surgery has further widened the horizon of minimally invasive surgery.

7.12.4 Cardiac Disorders

1. Atherosclerosis

Atherosclerosis is a disease in which plaque builds up inside the arteries. A plaque is made up of fat, cholesterol, calcium and other substances including cells (white blood cells, especially macrophages) found in the blood. Over time, the plaque hardens and narrows the arteries, limiting the blood flow through the arteries. There is also associated vasospasm. If the plaque ruptures, thrombosis and embolism could be precipitated.

Atherosclerosis can affect any artery in the body, including the heart, brain, arms, legs and pelvis. Different diseases can develop based on which artery is affected.

Pathophysiology The cause of atherosclerosis is not known. Certain conditions and habits can raise the risk of the disease. These are called risk factors. Factors like smoking; lack of physical activity, obesity, unhealthy diet, diabetes and hypertension, can be controlled, while age and family history cannot be controlled.

2. Coronary Heart Disease (CHD)

Coronary heart disease occurs when plaque builds up in the coronary arteries. The plaque narrows the arteries and reduces the blood supply to the heart muscle. Blood clots may also form in the arteries which could partially or completely block the blood flow.

Plaques can also form in the heart's smallest arteries. This is called Coronary Micro Vascular Disease (CMVD).

3. Angina

When blood flow to the heart muscle is reduced, it can lead to chest pain or angina, a strangling sensation in the chest or pressure and precipitated by exertion. It occurs due to myocardial ischemia.

4. Myocardial Infarction

Myocardial infarction, commonly known as heart attack, is an ischemia due to sudden interruption of blood supply to a part of the heart causing heart muscle cells to die. This is most commonly due to occlusion of a coronary artery following the rupture of a vulnerable atherosclerotic plaque in the wall of the artery. The resulting ischemia and oxygen shortage, if left untreated for a sufficient period of time, can cause damage and death (infarction) of heart muscle tissue (myocardium).

Symptoms are in the form of sudden chest pain, shortness of breath, weakness, palpitation, nausea, vomiting, sweating and anxiety. One fourth of all myocardial infarctions are silent without chest pain or any symptoms.

Pathophysiology The most common triggering event is the disruption of an atherosclerotic plaque in an epicardial coronary artery, which leads to formation of a clot and sometimes results in total occlusion of the artery. (See Fig. 7.39)

Plaque can become unstable, rupture and additionally promote a thrombus that occludes the artery—this can occur in minutes.

When a big plaque ruptures in the coronary vasculature, myocardial infarction results (heart attack). If the impaired blood flow to the heart lasts long, it triggers ischemic cascade and the heart muscle cells in the territory of the occluded coronary artery die.

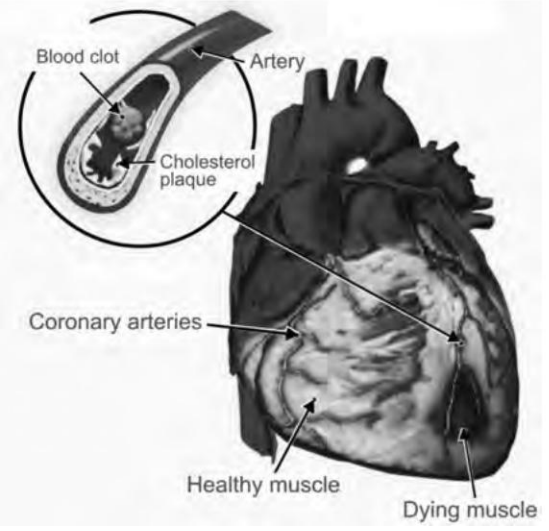


Fig. 7.39 *Condition of the heart in a heart attack*

5. Heart Failure

Heart failure is a condition in which the heart's function as a pump to deliver oxygen-rich blood to the body is inadequate to meet the body's needs.

Heart failure is almost always a chronic, long-standing condition, but it can sometimes develop suddenly.

The condition may affect the right side, the left side or both sides of the heart.

- **Right-sided heart failure** means that the right side of the heart cannot adequately pump venous blood into the pulmonary circulation. This causes a back-up of fluid in the body, resulting in swelling and edema especially of the feet, ankle and legs.
- **Left-sided heart failure** means the ability of the heart to pump blood forward—systemic circulation—from the left side of the heart, is decreased. Back-up behind the left ventricle causes accumulation of fluid in the lungs, leading to pulmonary edema.

In both types of heart failure, there is shortness of breath and tiredness.

The main **causes** of heart failure are coronary artery disease, high blood pressure and diabetes. Long-standing alcohol abuse and disorders of heart valves can also lead to heart failure. Less common causes are viral infections of the valves, thyroid disorders and cardiac arrhythmias.

Pathophysiology Reduced contractility or force of contraction, due to overloading of the ventricles causes the heart to function less. Failure of systole or diastole or both reduces stroke volume.

As the heart goes on working harder and harder to meet the metabolic demands, the amount the cardiac output can increase to meet this demand is reduced.

Enlargement of ventricles, due to the failing heart, causes a reduction in stroke volume due to mechanical and contractile inefficiency. In an attempt to improve contractility, there is hypertrophy of the myocardium which causes increased stiffness and decreased ability to relax during diastole.

6. Congenital Heart Disease

A Congenital Heart Defect (CHD) is a defect in the structure of the heart and great vessels of a newborn. Most defects either obstruct the blood flow in the heart or vessels or cause blood to flow through in an abnormal pattern.

Classification

When chambers are in Normal position and Sequence

A. **When shunting is predominant**—Atrial Septal Defect (ASD), Ventricular Septal Defect (VSD), atrioventricular septal defects and patent ductus arteriosus
B. **When stenosis or obstruction is predominant**—Absent atrioventricular connections like mitral and tricuspid atresia, absent or obstructed ventriculo-great arterial connections, obstructed great arteries like aortic atresia and coarctation of aorta, obstructed venous flow
C. **Anomalous valve position**—Ebstein's anomaly

When Chambers and Valves are not in Normal Sequence or Relationship

A. **Anomalies of relationship between atria and ventricles**—double-inlet with univentricle heart, atrioventricular discordance
B. **Anomalies between ventricles and great vessels**—Tetralogy of Fallot, truncus arteriosus, transposition of great vessels, double outlet right and left ventricles

Pathophysiology It may be due to intra-uterine developmental errors or failure of the heart and blood vessels to adapt to extra-uterine life.

7. Vascular Disorders

Arteriosclerotic vascular disease or arteriosclerosis affects the large and medium-sized arteries especially of the heart, brain and the lower extremities. Progressive narrowing and finally occlusion of the arteries causes vascular insufficiency. This causes functional disorders and is called **peripheral vascular disease**.

Pathophysiology The exact cause is not known but certain factors appear to predispose to its development. They are hypertension, diabetes, elevated cholesterol and smoking.

There can also be a genetic predisposition to this disorder.

There are certain conditions which can lead to arteritis of the large or medium arteries followed by occlusion or rupture. They are syphilis, bacterial infection and certain allergic disorders.

Certain conditions can involve the small arteries. It produces areas of local death and ulceration of the skin, particularly of the limbs. It is probably due to occlusion of the small arteries and loss of blood supply. These conditions are rheumatoid arthritis, lupus erythematosus, periarteritis nodosa and scleroderma.

8. Thrombosis

Thrombosis is the formation of a blood clot in a blood vessel. The vessel could be a vein or an artery. The clot is termed **thrombus**. It is initiated by platelets aggregation followed by fibrin formation in it. In the beginning, it is fragile and then it becomes solid. It obstructs the flow of blood.

There are two types of thrombosis:

- **Venous thrombosis** is a blood clot in a vein.
  One of the most common types of venous thrombosis is deep-vein thrombosis, where the clot forms in one of the deep veins in the lower limbs.
- **Arterial thrombosis** is a clot which forms in the artery. It often occurs in arteries that supply the heart or the brain.

9. Embolism

Sometimes a blood clot or a part of it migrates from one part of the body through the circulation and travels to another part, lodges there and causes blockage. This is known as **embolus**. There are various types of embolus—thrombo-embolism, cholesterol embolism, fat embolism, air embolism, septic embolism, amniotic fluid and foreign-body embolism. The commonest embolism is pulmonary embolism when a blood clot lodges in one of the lungs.

10. Varicose Veins

The most common disorder of the venous circulation is varicose veins. The most commonly involved veins are the greater and lesser saphenous. The veins get enlarged and tortuous.

Pathophysiology Normally, it develops due to loss of function of the valves in the superficial veins of the limbs. Involvement of superficial veins is called **primary varicose veins**; and if the deep venous system is involved it is called **secondary varicose veins**.

Varicose veins is mainly hereditary and occurs in members of the same family. It is more common in females than men.

It can develop in patients undergoing major surgery or in bedridden patients who have been immobile for a long time. Thrombosis of veins in the legs occurs, especially in the deep veins of the calf.

11. Hypertension

Hypertension is the persistent increase in blood pressure. Blood-pressure readings are measured in millimeters of mercury (mmHg). Till recently, the upper level of BP was taken as 140/90 mmHg. Of late, however, the recommended normal BP in an adult is 120/80 mmHg.

120–139/80–89	Prehypertension
140–159/90–99	Stage 1 hypertension
>160/>100	Stage 2 hypertension

The upper reading is the systolic blood pressure, which corresponds to the force against the walls of the arteries as the left ventricle contracts and pumps blood into the aorta. It is a lateral pressure of the blood column against the wall of the vessels.

The lower reading is the diastolic pressure, which represents the pressure in the arteries as the heart relaxes after the contraction. It reflects the lowest pressure to which the arteries are exposed.

Hypertension is of two types—primary (essential or idiopathic) and secondary hypertension.

(a) Essential or Primary Hypertension It accounts for 85 to 90% of hypertension cases. Depending on the level of hypertension and the progression of the disease, it is divided into two types:

A. Benign Hypertension The blood pressure level is mild to moderate and progresses slowly.

Arteriosclerosis contributes to increase in the blood pressure and is seen with advancing age. The basic causes or underlying defects are not always known. Yet, several factors combine to raise the blood pressure or act as predisposing factors.

It develops in groups or societies who consume more salt, exceeding 5.8 grams daily.

Other factors are obesity, excessive alcohol intake, hereditary (genetic) susceptibility, cigarette smoking, kidney failure and lack of exercise.

B. Malignant Hypertension The blood pressure is high and rises very rapidly. Diastolic goes above 120 mm of Hg. It can lead to serious consequences like retinopathy, encephalopathy, renal failure and cardiac failure.

(b) Secondary Hypertension Secondary hypertension is caused by another medical condition or medication and accounts for 10 to 15% of cases of hypertension. There is a specific abnormality in one of the organs or systems. It could be due to kidney diseases, alcohol abuse, auto-immune disorders, endocrine disorders, coarctation of aorta, diabetes and certain medications.

Pathophysiology In kidney diseases, raised blood pressure is probably due to the constrictor effect of excess renin released by the diseased kidney.

In adrenal cortex disorders, excessive secretion of aldosterone and cortisol stimulates the retention of excess sodium and water, which increases the blood volume and blood pressure.

In adrenal medulla disorders, secretion of adrenaline and nor adrenaline raises the blood pressure as seen in pheochromocytoma.

In coarctation of aorta, there is rise in blood pressure in the vessels proximal to the coarctation.

Hypertension is a side effect or complication of certain drugs—corticosteroids, oral contraceptives, nonsteroidal anti-inflammatory drugs, etc.

12. Hypotension

Hypotension is the persistent decrease in blood pressure (systolic falls below 90 mmHg and diastolic falls below 50 mmHg). It has to be considered in context of the person's previous level of blood pressure.

This usually occurs as a complication of some other condition like hemorrhage, shock, burns, Addison's disease, etc.

Postural hypotension is a situation where there is fall in blood pressure on standing upright from the recumbent position. It is seen usually in older people. It could be due to delayed response of the baroreceptors to maintain the pressure. It is also seen when the person is on antihypertensive drugs.

REVIEW QUESTIONS

1. Write a note on the external structure of the heart.
2. Describe the internal structure of the heart with labeled diagram.
3. Explain and draw the structure of the valves of the heart.
4. Describe various properties of the heart. Describe the conducting system with a diagram.
5. Explain the cardiac cycle in detail. Illustrate various stages.
6. What is cardiac output? Explain the factors affecting cardiac output.
7. Define systolic and diastolic blood pressure. Describe how blood pressure is regulated. How is it measured?
8. Write a note on various cardiac arrhythmias.
9. Name the various types of circulation. Write a note on pulmonary circulation.
10. Describe coronary circulation.
11. Write short notes on:
    a. ECG
    b. Heart sounds
    c. Factors affecting heart rate
    d. Pericardium
    e. Venous drainage of the heart
    f. Anastomosis and end arteries
    g. Difference between arteries and veins
    h. Arterial pulse
    i. Venous pulse
    j. Physiological variation in blood pressure
    k. Coronary circulation
    l. Investigative modalities in cardiology
    m. Portal circulation

Chapter

8 Respiratory System

- **ANATOMY**
  - **Nose and nasal cavity**
    - **Structure**
      - **Lining of the nose**
      - **Nasal communication**
    - **Functions**
    - **Applied anatomy**
  - **Pharynx**
    - **Nasopharynx**
    - **Oropharynx**
    - **Laryngopharynx**
    - **Structure**
      - **Mucus membrane layer**
      - **Fibrous tissue layer**
      - **Muscle tissue layer**
      - **Arterial supply**
      - **Venous drainage**
      - **Nerve supply**
    - **Functions**
    - **Applied anatomy**
  - **Larynx**
    - **Relations with the surrounding structures**
    - **Structure**
      - **Thyroid cartilage**
      - **Cricoid cartilage**
      - **Arytenoid cartilage**
      - **Epiglottis**
      - **Vocal cords**
      - **Arterial supply**
      - **Venous drainage**
      - **Nerve supply**
    - **Functions**
    - **Applied anatomy**

- Trachea
  - Relations with the surrounding structures
  - Structure
    - Arterial supply
    - Venous drainage
    - Lymphatic drainage
    - Nerve supply
  - Functions
  - Applied anatomy
- Bronchi and smaller air passages
  - Right bronchus
  - Left bronchus
  - Structure
    - Arterial supply
    - Venous drainage
    - Lymphatic drainage
    - Nerve supply
- Respiratory bronchioles and alveoli
- Lungs
  - Structure
    - Apex
    - Base
    - Ant.border
    - Posterior border
    - Inferior border
    - Costal surface
    - Medical surface
    - Arterial supply
    - Venous drainage
    - Lymphatic drainage
    - Nerve supply
  - Bronchopulmonary segments
  - Applied anatomy
- Mediastinum
- Pleura and pleural cavity
  - Applied anatomy
- Pulmonary circulation

• PHYSIOLOGY

- Mechanism of respiration
  - Diaphragm
  - Muscles of respiration
  - Movements of the lungs
    - Inspiration
    - Expiration
  - Factors affecting normal respiration
    - Elasticity

- Compliance
- Air flow resistance

- **Regulation of respiration**
  - Nervous mechanism
  - Chemical mechanism
    - Chemoreceptors
      - Central
      - Peripheral

- **Respiratory reflexes**
  - Hering-Breuer Reflex
  - Impulses from 'J'
    - Role of baroreceptors
    - Impulse from Irritant
    - Response to pain
    - Cough and Sneeze

- **Principles of gas exchange**
  - External respiration
  - Internal respiration
  - Transport of oxygen
  - Transport of carbon dioxide
  - Chloride shift

- **Pulmonary volumes**
  - Lung volumes
    - Tidal volume
    - Inspiratory reserve volume
    - Expiratory reserve volume
    - Residual volume
  - Measurement of lung volumes
  - Pulmonary capacities
    - Inspiratory capacity
    - Functional residual capacity
    - Total lung capacity
    - Vital capacity
      - Physiological variations
      - Pathological variations
    - Forced expiratory volume
    - Alveolar ventilation

- **Pulmonary function tests**
  - Spirometry
    - Helium dilution technique
    - Nitrogen washout method

- **Artificial Respiration**

- **Methods**
  - Manual methods
    - Mouth to mouth method
    - Holger Nielsen method
  - Mechanical methods
    - Drinker's method
    - Ventilation method

- Hypoxia

ABNORMAL TYPES OF BREATHING

- Dyspnoea
- Cheynes-stokes breathing
- Apnea
- Cyanosis
- Asphyxia

RESPIRATORY DISORDERS

- Pharyngitis
- Laryngitis
- Bronchitis
- Tuberculosis
- Chronic obstructive lung disease
- Asthma
- Emphysema
- Bronchiectasis
- Pneumonia
- Lung abscess
- Pleural effusion
- Pneumothorax
- Carcinoma of the lung

Introduction

The human body is made up of different systems. The ultimate unit of each system is the cell. The cells need energy to carry out their various activities, which is derived from bio-chemical reactions that can take place only in the presence of oxygen (O_2). The waste product released is carbon dioxide (CO_2).

The respiratory system is the mediator for providing O_2 from atmospheric air and throwing away CO_2 from the body.

It also helps in losing heat through the expired air. Water vapour is also lost through the expired air to some extent.

The respiratory system plays an important role in maintaining homeostasis. By balancing excretion of CO_2, body pH is maintained.

8.1 ANATOMY

The organs of the respiratory system are the nose, pharynx, larynx, trachea, two bronchi (one bronchus to each lung), bronchioles and smaller air passages, two lungs and their coverings—the pleura, muscles of respiration, the intercostal muscles and the diaphragm.

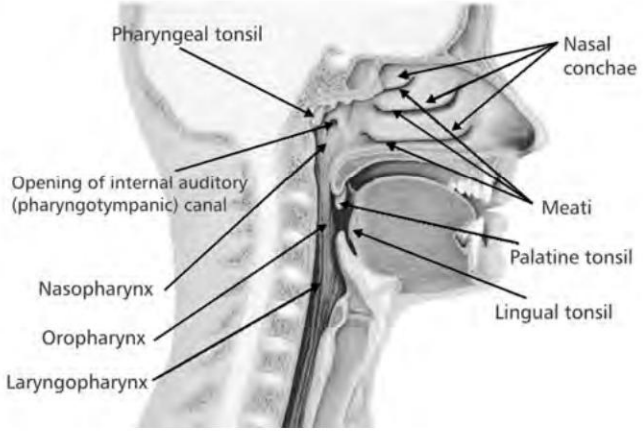


Fig. 8.1 *Upper respiratory tract*

The respiratory tract is divided into 2 parts:

1. **Upper respiratory tract** which extends from the external nares to the vocal cord
2. **Lower respiratory tract** which extends from the vocal cord to the alveoli.

The respiratory tract is studied in 2 zones:

1. Conducting zone
2. Respiratory zone

The conducting zone is up to the level of terminal bronchioles.

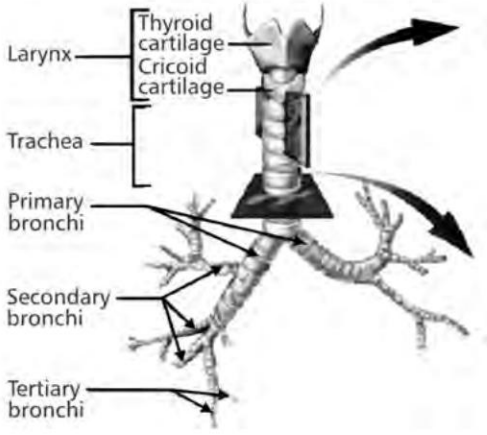


Fig. 8.2 *Lower respiratory tract*

The respiratory zone are the alveolar ducts and the alveoli.

8.1.1 Nose and Nasal Cavity

1. Structure

The nasal cavity is the first of the respiratory organs. It consists of a large irregular cavity which is divided by a septum. The septum consists of the anterior part, which is formed by hyaline cartilage; and the posterior part which is bony and is formed by the perpendicular plate of the ethmoid bone and the vomer.

The roof is formed by the cribriform plate of the ethmoid bone, the sphenoid bone, frontal bone and the nasal bones.

The roof of the mouth forms the floor. The front of the floor is formed by the hard palate anteriorly and the soft palate posteriorly. The hard palate consists of the maxilla and palatine bones. The soft palate consists of involuntary muscles.

The medial wall is formed by the septum.

The lateral wall is formed by the maxilla, the ethmoid bone and the inferior conchae.

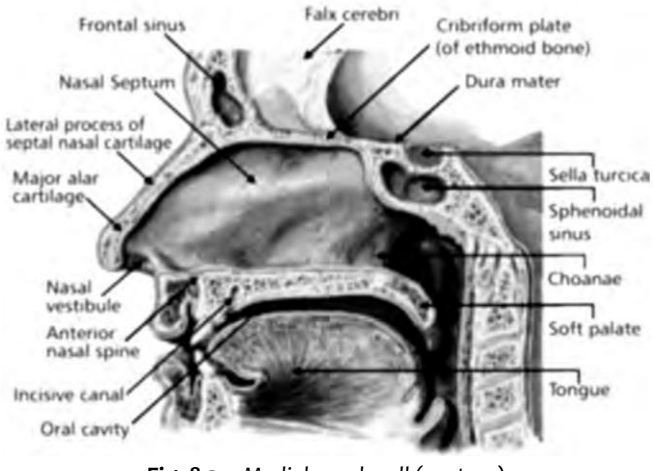


Fig. 8.3 *Medial nasal wall (septum)*

The posterior wall is actually the posterior wall of the pharynx.

(a) Lining of the Nose The nose is lined with ciliated mucous membrane which is very vascular and contains mucous-secreting goblet cells. At the anterior nares, the mucous membrane of the nose blends with the skin of the face and posteriorly it becomes the nasal part of the pharynx.

(b) Nasal Communications There are certain communications with the nasal cavity through certain openings:

1. The anterior nares open into the exterior and are also called **nostrils**. Hairs are present here.
2. The nasal cavity communicates with the pharynx through the posterior nares.
3. The paranasal sinuses are cavities in the bones of the face and cranium. They contain air and open into the nose, and thus there are connections between the sinuses and the nasal cavity through these small openings. The mucous membrane lining the sinuses is continuous with the mucous membrane of the nasal cavity.

The following are the main paranasal sinuses:

In the lateral wall is the maxillary sinus, in the roof are situated the frontal and sphenoidal sinuses, while in the upper part of the lateral wall are present many small ethmoidal sinuses.

2. Functions

1. The air which is inspired is warmed, filtered and moistened (humidified) in the nose.
   Warming of the air is due to good vascularity of the nasal mucosa.
2. Filtering and cleaning of air is done by the hairs at the anterior nares. Dust particles and microbes adhere to the mucous. Beating of cilia, found in the mucosa, pushes the mucous towards the throat, where it is expectorated or swallowed.
3. Humidification of air is done by the moist mucosa.
4. The surface area of the nasal cavity is increased due to the projecting conchae, so that it becomes easy and better for the nose to carry out its functions fast.
5. Irritation of nasal mucosa by any foreign material causes sneezing, so that the irritant gets expelled.
6. Besides these functions, the nose has a very important function to carry out. It is the organ of the sense of smell. Nerve endings located in the roof of the nose are stimulated by odorous materials. Impulses are conveyed to the brain by the olfactory nerves and sensation of smell is perceived.

3. Applied Anatomy

1. Common cold is the commonest disease of the nose.
2. Paranasal sinuses get infected from infection of the nose. Maxillary sinusitis is the commonest among them.
3. Hypertrophy of mucosa occurs due to allergy, causing sneezing, nasal block and watery discharge.
4. Relations of the nose to anterior cranial fossa are important because infection in the nose could lead to the spread of infection to the brain.

8.1.2 Pharynx

The pharynx extends from the base of the skull to the level of the 6th cervical vertebra. It is 12 to 14 cm long and lies behind the nose, mouth and larynx. The pharynx is wider at its upper end.

Superiorly, it is related to the inferior surface of the base of the skull. Inferiorly, it is continuous with the esophagus. Anteriorly lie the openings of nose, mouth and larynx, while posteriorly lie the bodies of the first 6 cervical vertebrae, the areolar tissue and involuntary muscles covering the vertebral bodies.

On the basis of its location, the pharynx can be divided into

- Nasopharynx
- Oropharynx
- Laryngopharynx

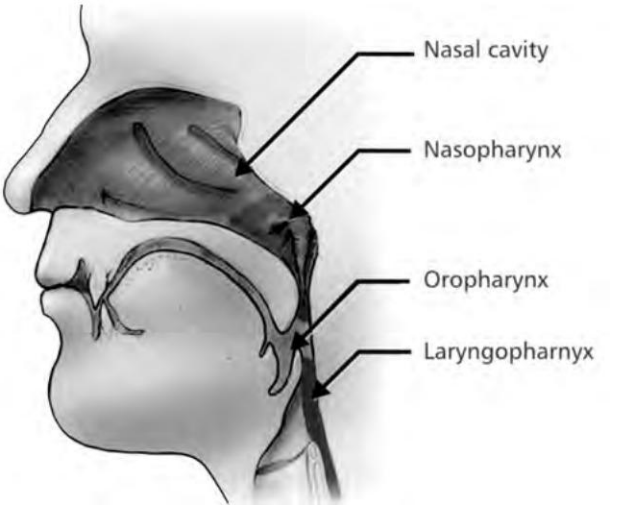


Fig. 8.4 *Pharynx*

(a) Nasopharynx The nasopharynx lies behind the nose above the level of the soft palate. The auditory tubes (Eustachian tube) open on its lateral walls.

On the posterior wall of the nasopharynx there are the adenoids consisting of lymphoid tissue and which are seen best in children up to 7 to 8 years of age. Then they atrophy.

(b) Oropharynx The oropharynx lies behind the mouth and hence it is so named.

It extends from below the level of the soft palate up to the upper part of the body of the 3rd cervical vertebra.

The lateral walls along with the soft palate form two folds (tonsillar fossa) between which are found the palatine tonsil, one on each side.

The nasopharynx and oropharynx are separated by the soft palate and uvula.

(c) Laryngopharynx The laryngopharynx extends from 3rd to 6th cervical vertebra.

The oropharynx extends as the laryngopharynx and is continued below as the oesophagus.

1. Structure

The pharynx is made up of 3 layers:

From inside to outside, these are

- Mucous membrane layer
- Fibrous tissue layer
- Muscle tissue layer

(a) Mucous Membrane Layer The mucous membrane lining in the nasopharynx consists of ciliated columnar epithelium and is continuous with the mucosa of the nose.

In the oropharynx and laryngopharynx, it is formed by striated squamous epithelium and is continuous with the lining of the mouth and oesophagus.

(b) Fibrous Tissue Layer Fibrous tissue layer forms the intermediate or the middle layer.

It is thicker in the upper part of nasopharynx because the muscle layer is thin and is thinner in the lower part of nasopharynx because here the muscle layer is thicker.

(c) Muscle Tissue Layer The muscle layer consists of several involuntary constrictor muscles. They help in deglutition (swallowing).

The upper end of the pharynx is closed by the lower constrictor muscles which open only during swallowing.

(d) Arterial Supply The pharynx is supplied by the branches of the facial artery.

(e) Venous Drainage Venous return is into the facial and internal jugular veins.

(f) Nerve Supply The pharynx is supplied by the pharyngeal plexus. It has both parasympathetic and sympathetic supplies.

- Parasympathetic supply is by the vagus and glossopharyngeal nerves.
- Sympathetic supply is by the nerves from the superior cervical ganglia.

2. Functions

1. The pharynx does the function of warming and humidification of the inhaled air.
2. The olfactory nerve carrying fibers of the sense of taste, ending in the epithelium of the oral and pharyngeal parts, give the sense of taste.
3. The pharynx is the common passageway for air and food.

   The pharynx is an organ connected, both, with the respiratory system and the digestive system. Air passes through the nasal and oral parts and food passes through the oral and laryngeal parts.

   Thus, it is the common passage for food and air.
4. **Hearing**—The auditory tube extends from the nasal part of the pharynx to middle ear, on both the sides and allows air to enter into the middle ear.

   Hearing depends on presence of air on both the sides of the tympanic membrane.
5. **Protection**—The lymphatic tissues present in the pharyngeal tonsils defend against infection.
6. **Speech**—Pharynx acts as a resonating chamber for the sound ascending from the larynx and gives resonance and depth to the voice.

3. Applied Anatomy

1. Tonsils are large in children and decrease in size after puberty.
2. Tonsils are frequently the site for infection which may spread to surrounding tissue forming a peritonsillar abscess.
3. Enlarged and infected tonsils often require removal.
4. Difficulty in swallowing is known as **dysphagia**.
5. **Pharyngeal diverticulum** is a pouch protruding from the wall of the pharynx.

8.1.3 Larynx

The larynx extends from the root of the tongue and the hyoid bone up to the trachea. It is also called the **voice box**. Posteriorly, lies the laryngopharynx at the level of 3rd to 6th cervical vertebrae. The size of the larynx, till puberty, is the same in males and females but after puberty, it grows bigger in males. This gives rise to the deeper voice in males.

1. Relation to the Surrounding Structures

Superiorly, it is related to the hyoid bone and the root of the tongue.

Inferiorly, it is continuous with the trachea.

Anteriorly, it is related to the muscles of the neck and the muscles attached to the hyoid bone.

Posteriorly lie the laryngopharynx and 3rd to 6th cervical vertebrae.

Laterally lie the lobes of the thyroid gland, one on each side.

Fig. 8.5 *Anatomy of larynx*

2. *Structure*

The larynx consists of vocal cords and several irregularly shaped cartilages. They are attached to each other by ligaments and membranes. They are

- 1 thyroid cartilage
- 1 cricoid cartilage
- 2 arytenoid cartilages
- 1 epiglottis

The first three are hyaline cartilage and epiglottis is an elastic fibrocartilage. (See Fig. 8.5).

(a) Thyroid Cartilage

The thyroid cartilage is the most prominent of all these structures. It consists of two flat pieces of hyaline cartilage. Anteriorly, these two pieces are fused. This prominence is called the Adam's apple. Just above the prominence, the laminae are separated forming a V-shaped notch called the **thyroid notch**. Posteriorly, the cartilage does not fuse but remains incomplete. The posterior border extends upwards and downwards to form processes called superior and inferior cornu.

On the inner side, striated squamous epithelium lines the upper part of the cartilage which is similar to the larynx, and the lower part is lined with ciliated columnar epithelium, like the trachea. The external surface gives attachment to muscles.

(b) Cricoid Cartilage The cricoid cartilage lies below the thyroid cartilage. It is also composed of hyaline cartilage. It encircles the larynx completely and is shaped like a signet ring. The anterior part is narrow while the posterior part is broad. The posterior part of the cartilage articulates with the arytenoid cartilages above, and below it articulates with the inferior cornu and thyroid cartilage. It is lined with ciliated columnar epithelium. Muscles and ligaments are attached to its outer surface.

The upper respiratory tract ends at the level of the lower border of this cartilage.

(c) Arytenoid Cartilage The arytenoid cartilages are also hyaline cartilages and they are shaped like a pyramid. They are

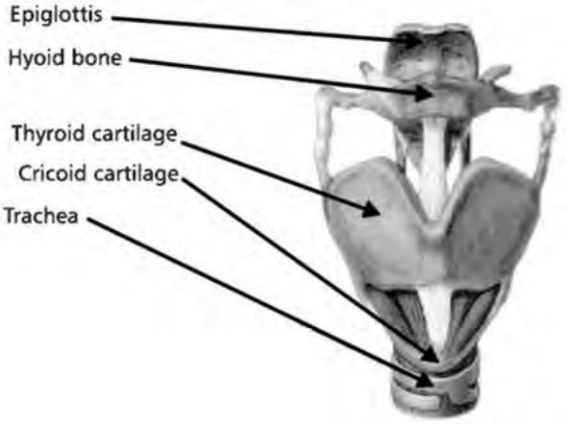


Fig. 8.6 *Cartilages of larynx*

two in number and lie on top of the broad part of the cricoid cartilage. A part of the posterior part of the larynx is formed by this cartilage. They are lined by ciliated columnar epithelium. They give attachment to vocal cords and muscles.

(d) Epiglottis The epiglottis is shaped like a leaf. It is a fibro-elastic cartilage and is attached to the inner surface of the anterior wall of the thyroid cartilage. It extends obliquely towards the tongue and is covered with striated squamous epithelium. The epiglottis covers the larynx during swallowing so that food which comes here does not enter the larynx but enters the oesophagus and the lungs are thus protected.

Several ligaments and membranes join the cartilages to each other and connect the cartilages to the hyoid bone.

(e) Vocal Cords Inside the larynx there are two vocal cords made up of mucous membrane. They have cordlike edges and extend from the inner wall of thyroid prominence anteriorly to the arytenoid cartilage posteriorly.

Muscles control the functioning of the vocal cords. When the muscles relax, the vocal cords move apart and the passage opens up. There is vibration of the vocal cords and the pitch of the sound is low. This movement of the vocal cords

is called **abduction**. The muscles contract and the vocal cords get adducted and they vibrate due to passage of air from the lungs. This produces a high-pitched sound. So, pitch of the voice depends on the stretch produced on the vocal cords by the muscles.

(f) Arterial Supply The various parts of the larynx are supplied by superior and inferior laryngeal arteries.

(g) Venous Drainage Blood drains into the thyroid veins which join the internal jugular vein.

(h) Nerve Supply The different structures of the larynx are supplied by parasympathetic fibers coming from superior laryngeal and recurrent laryngeal nerves, which are branches of the vagus nerve.

3. Functions

1. The larynx produces sound.
   Sound has pitch, volume and resonance.
   (a) **Pitch**—Pitch of the voice depends upon the tension applied to the vocal cords. At puberty, the pitch of the adult male voice is lower due to longer size of the vocal cords.
   (b) **Volume**—Volume depends upon the force with which the cords vibrate. The cords vibrate more when there is greater force of expired air, and louder sound is produced.
   (c) **Resonance**—Resonance depends on certain factors like the air in the paranasal sinuses, the shape of the mouth, position of the tongue and lips and the action of the facial muscles.
2. When the air passes through the larynx, it humidifies, filters and warms the inspired air as it travels through it.
3. Speech is possible during expiration when the sounds produced by the vocal cords are adjusted by the tongue, cheeks and lips.
4. The larynx acts as a passage between the pharynx and trachea to allow the air to pass.
5. It protects the lower respiratory tract:
   During swallowing, the larynx moves upwards and the epiglottis covers the air passage, so that food which has entered here passes into the esophagus and not into the trachea.

4. Applied Anatomy

1. When any foreign object enters the larynx, there is severe coughing so that the object is expelled. But when there is damage to the internal laryngeal nerve, there is anesthesia of the mucous membrane in the supraglottic part of the larynx. So the foreign bodies easily enter the larynx as stimulation does not take place.
2. Damage to external laryngeal nerve causes weakness of phonation.
3. When both the recurrent laryngeal nerves are damaged, phonation is completely lost as the vocal cords lie in between abduction and adduction position.
4. The larynx can be examined either directly or indirectly. **Direct laryngoscopy** is done using a laryngoscope. **Indirect laryngoscopy** is done using a laryngeal mirror. Direct laryngoscopy requires the use of anesthesia. By both these methods the following structures can be examined—base of the tongue, epiglottis, aryepiglottic folds, vestibular folds, pyriform fossa and the vocal cords.
5. As the larynx is the narrowest part of the respiratory passage, foreign bodies get stuck up here commonly, leading to obstruction to the passage.
6. Infection of larynx is called **laryngitis** and it causes hoarseness of voice.
7. Laryngeal edema occurs due to many diseases and can cause obstruction to breathing.

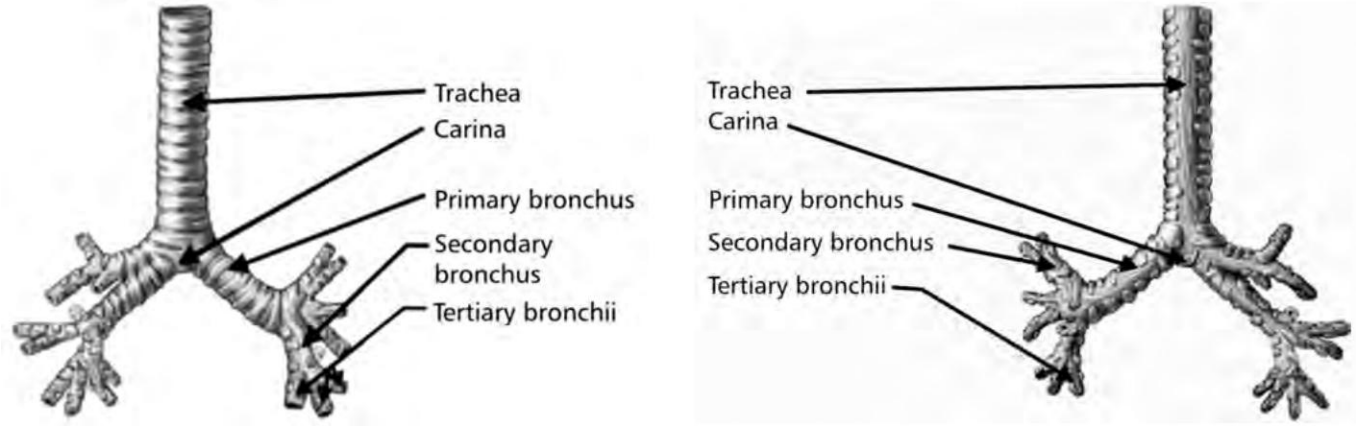
8.1.4 Trachea

The trachea is a wide tube lying more or less in the midline, in the lower part of the neck and in the superior mediastinum. Its upper end is continuous with the lower end of the larynx while the lower end divides into right and left principal bronchi.

The trachea is 10 to11 cm long and lies in the median plane in front of the esophagus.

1. Relations with the Surrounding Structures

Anteriorly	:	Manubrium sterni
		Sternothyroid muscles
		Remains of the thymus
		Aortic arch
		Isthmus of thyroid gland
		Deep cardiac plexus
		Lymph nodes
Posteriorly	:	Esophagus
		Vertebral column
Superiorly	:	Larynx
Inferiorly	:	Right and left bronchi
On the right side	:	Right lung and pleura
		Right vagus
		Lobe of thyroid gland
		Azygos vein
On the left side	:	Arch of aorta
		Left common carotid
		Left subclavian arteries
		Lobe of thyroid gland
		Left recurrent laryngeal nerve



(a) Anterior view (b) Posterior view

Fig. 8.7 *Trachea*

2. Structure

The trachea has a fibro-elastic wall supported by a cartilaginous skeleton which is formed by C-shaped rings. The rings are 16 to 20 in number. Posteriorly, the C-shaped ring is incomplete and there is a gap which is closed by a fibro-elastic membrane and involuntary muscles. This posterior wall is in relation to the esophagus.

There are three layers of tissue which cover the cartilages.

- The outer layer consists of fibrous and elastic tissue.
- The middle layer is made up of cartilages and smooth muscle and winds round in a helical arrangement. Blood vessels and lymph vessels are found in this layer of areolar tissue.
- The inner layer contains ciliated columnar epithelium. It has goblet cells which secrete mucous.

(a) Arterial Supply Blood supply is by the inferior thyroid and bronchial arteries.

(b) Venous Drainage Blood drains into the inferior thyroid vein which in turn drains into the bronchocephalic vein.

(c) Lymphatic Drainage Lymphatic drainage is into the pretracheal and paratracheal nodes.

(d) Nerve Supply The trachea is supplied by parasympathetic and sympathetic nerves.

Parasympathetic supply is through the recurrent laryngeal nerve. It is sensory and secretomotor to the mucous membrane and motor to the trachealis muscle.

Sympathetic supply comes from the middle cervical ganglia.

3. Functions

1. Warming, humidifying and filtering of inhaled air continues as it reaches here.
2. Due to the arrangement of cartilages and elastic tissue, the trachea remains patent and does not kink during movements of the neck.
   The tracheal cartilage is incomplete posteriorly; this facilitates it to dilate and allows the esophagus to indent the trachea during swallowing. Also, due to the cartilages, at the end of forced expiration, the trachea does not collapse.
3. Due to the movement of the cilia, the mucous with the adherent particles is pushed towards the larynx, where it is swallowed or expectorated. This is called mucocilliary escalator.
4. **Cough reflex**—Nerve endings in the trachea get stimulated when irritated and impulses are conducted via vagus nerve to the respiratory centre in the brain stem. There is a reflex motor response and the person takes a deep inspiration. There is closure of the glottis. Abdominal and respiratory muscles contract at this moment and there is sudden release of air. Due to this pressure, mucous along with the foreign body is expelled.
   This is what we call the cough reflex.

4. Applied Anatomy

1. In X-ray photographs, the trachea is seen as a vertical translucent shadow in front of the cervicothoracic spine.
2. The trachea can be palpated in the suprasternal notch; it is median, i.e., central in position. Shift of the trachea indicates a mediastinal shift.
3. During swallowing, when the larynx is elevated, the trachea elongates at its upper end by stretching, because the tracheal bifurcation cannot move. Any downward pull will produce the physical sign which is known as **tracheal tug**.

4. Tracheotomy (making a hole in the trachea) is an emergency procedure done during acute breathing difficulty or when the patient may have to be put on a ventilator.
5. Mucous secretions help in trapping inhaled foreign particles and the soiled mucous is then expelled by coughing. Cilia of the mucous membrane beat upwards, pushing up the mucous towards the pharynx.
6. Trachea may get compressed by enlargement of thyroid, thymus, aortic arch and lymph nodes. This can cause irritating dry cough, breathlessness and sometimes a husky voice.

8.1.5 Bronchi and Smaller Air Passages

The trachea divides into two primary bronchi, the right bronchus and left bronchus.

(a) Right Bronchus The right bronchus is wider, shorter and more vertical than the left bronchus. It is 2.5 cm long. In the lung it divides into three branches. Each branch then subdivides into many smaller branches. Any foreign body entering the trachea is more prone to enter this bronchus as it is more vertical.

(b) Left Bronchus The left bronchus is narrower than the right. In the lung it divides into two branches which further divide into several branches. It is longer than the left bronchus and is 5 cm in length.

1. Structure

The structure of bronchi is the same as that of the trachea. Bronchi divide into bronchioles. The bronchioles divide into terminal bronchioles which further divide into respiratory bronchioles. The respiratory bronchioles finally form alveolar ducts which end as alveoli. Near the distal end, the cartilages become irregular. They are absent in the final bronchioles. Where the cartilages are absent, the smooth muscles become thicker. In the distal bronchioles, the mucous membrane becomes nonciliated, and has cuboidal-shaped cells.

(a) Arterial Supply Blood supply is by right and left bronchial arteries.

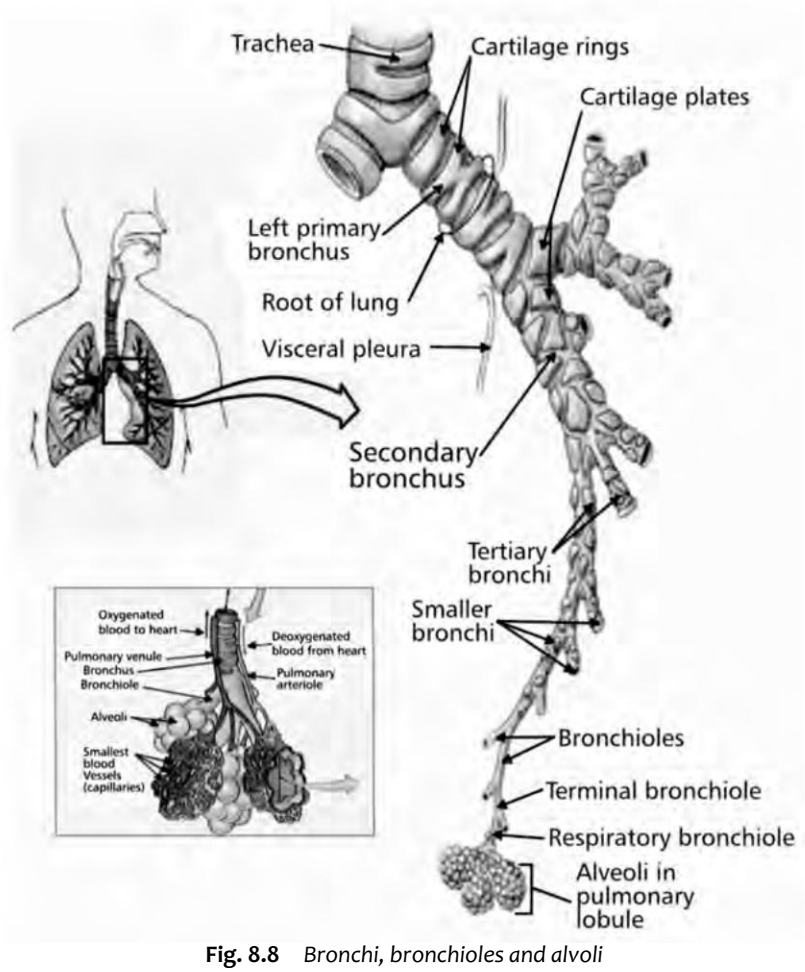


Fig. 8.8 *Bronchi, bronchioles and alvoli*

(b) Venous Return Blood returns mainly through bronchial veins to azygos vein on the right side and superior intercostal vein on the left side.

(c) Nerve Supply The bronchioles are supplied, both, by parasympathetic and sympathetic fibers.

Parasympathetic supply is from vagus nerve which is responsible for broncho constriction.

Sympathetic fibers cause bronchodilation.

(d) Lymphatic Drainage Lymph drains into a fine network of lymph vessels, which drain into lymph nodes near the hilum. From here it drains into the thoracic duct on the left side and right lymphatic duct on the right.

8.1.6 Respiratory Bronchioles and Alveoli

Distal to the terminal bronchioles are lobules which are the blind ends of the respiratory tract. They consist of respiratory bronchioles, alveolar ducts and alveoli. Gradually, the wall thins out. Finally, there is only a single layer of simple squamous epithelial cells in the alveolar ducts and alveoli. The alveoli are surrounded by a network of capillaries. Gas exchange takes place across the alveolar and capillary membranes.

There is a network of elastic connective tissue in between the alveoli and capillaries. Macrophages, fibroblasts, nerves, blood vessels and lymph vessels are seen in this loose tissue.

There are certain cells in the connective tissue which secrete surfactant, which prevents the alveoli from drying out. The surfactant also reduces surface tension. This prevents the alveolar walls from collapsing during expiration.

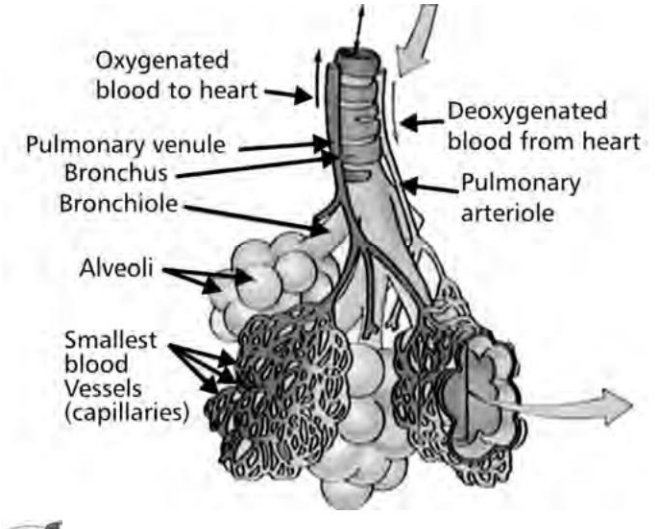


Fig. 8.9 *Alveoli (Refer colour figure)*

8.1.7 Lungs

The lungs are a pair of respiratory organs situated in the thoracic cavity. Each lung invaginates the corresponding pleural cavity. The two lungs are separated by the mediastinum.

The lungs are spongy in texture. The right lung weighs 625 gms and is about 50 gms heavier than the left lung.

1. Structure

Each lung is conical in shape and has

1. An apex at the upper end
2. A base resting on the diaphragm
3. Three borders—anterior, posterior and inferior
4. Two surfaces—costal and medial

(a) Apex The apex is blunt and rounded and rises into the root of the neck. It reaches an inch above the middle 1/3rd of the clavicle. The first rib, blood vessels and nerves found in the root of the neck are in relation to the apex.

(b) Base The base is semilunar and concave. It rests on the diaphragm which separates the right lung from the right lobe of the liver and left lung from the left lobe of the liver, fundus of the stomach and spleen.

(c) Anterior Border The anterior border is very thin and shorter than the posterior border. On the right side it is vertical. On the left side, there is a wide cardiac notch below the level of

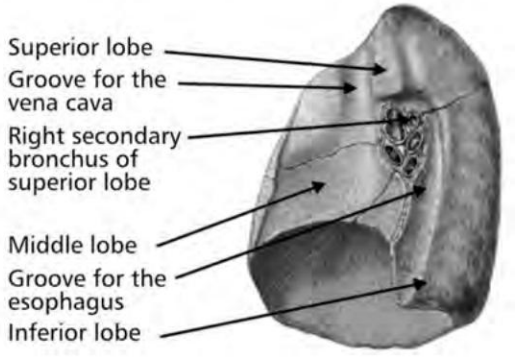


Fig. 8.10 *Structures related to the mediastinal surface of the right lung*

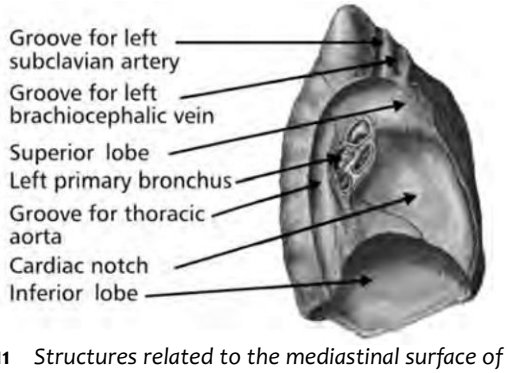


Fig. 8.11 *Structures related to the mediastinal surface of the left lung*

4th costal cartilage. The heart and pericardium are uncovered by the lung in the region of this notch.

(d) Posterior Border The posterior border is thick and ill-defined. It corresponds to the medial margins of the heads of the ribs.

(e) Inferior Border The inferior border separates the base of the lung from the costal and medial surfaces.

(f) Costal Surface The costal surface is large and convex. It is in contact with costal cartilages, ribs and intercostal muscles.

(g) Medial Surface The medial surface is concave. In the center of this surface, there is a roughly triangular shaped area which is called the **hilum**. There are certain structures which enter and leave the lung at the hilum. They are the pulmonary artery, pulmonary veins, bronchus, bronchial artery, bronchial veins, the lymph vessels and nerves. The medial surface is divided into anterior or mediastinal part, and posterior or vertebral part.

The mediastinal part is related to the mediastinal septum.

The vertebral part is related to the vertebral bodies, intervertebral discs and the posterior intercostals vessels.

Table 8.1 *Structures related to the right and left lungs*

Right Lung	*Left Lung*
1. Right atrium and auricle infundibulum,	1. Left ventricle, Left auricle and adjoining part of right ventricle
2. A small part of right ventricle	2. Pulmonary trunk
3. Superior vena cava	3. Arch of aorta
4. Lower part of right brachio cephalic vein	4. Descending thoracic aorta
5. Azygos vein	5. Left subclavian artery
6. Esophagus	6. Thoracic duct
7. Inferior vena cava	7. Esophagus
8. Trachea	8. Left brachio cephalic vein
9. Right vagus nerve	9. Left vagus nerve
10. Right phrenic nerve	10. Left phrenic nerve
	11. Left recurrent laryngeal nerve

Table 8.2 *Differences between the right and left lungs*

Right Lung	*Left Lung*
1. Has two fissures	1. Has only one fissure
2. Has three lobes	2. Has two lobes
3. Anterior border is straight	3. Anterior border is interrupted by the cardiac notch
4. Larger and heavier	4. Smaller and lighter
5. Weight is 625 g	5. Weight is 575 g
6. Shorter and broader	6. Longer and narrower

The right lung is divided into 3 lobes—superior, middle and inferior lobes—by two fissures. The left lung is divided into two lobes—superior and inferior—by the oblique fissure.

The lungs expand maximally in the inferior direction as the movements of thoracic wall and diaphragm are maximal towards the base of the lung. The presence of oblique fissure allows a more uniform expansion of the whole lung.

(h) Arterial Supply The bronchial arteries supply nutrition to the bronchial tree and pulmonary tissue.

The pulmonary artery divides into two branches. It brings deoxygenated blood to each lung. Inside the lung, it divides into many branches and finally forms a dense capillary network around the alveoli. There is only one layer of flattened epithelial cells in the walls of alveoli and capillaries. Gaseous exchange takes place between air in the alveoli and blood in the capillaries across the two membranes.

Oxygenated blood is returned to the heart by the pulmonary veins.

There are precapillary anastomoses between bronchial and pulmonary arteries. These connections enlarge when any one of them is obstructed in disease.

(i) Venous Drainage From bronchi, blood drains into the bronchial veins and from the lungs is drained by pulmonary veins.

(j) Lymphatic Drainage There are two sets of lymphatics.

- **Superficial vessels** drain the peripheral lung tissue and run round the border and reach the hilum.
- **Deep vessels** drain the bronchial tree, the pulmonary vessels and connective tissue. They also run towards the hilum and drain into bronchopulmonary nodes.

(k) Nerve Supply Nerve supply is by both parasympathetic and sympathetic fibers.

Parasympathetic supply is by the vagus nerve.

It has three components—motor, sensory and secretomotor.

The motor part is responsible for bronchospasm.

The sensory part is responsible for stretch reflex which initiates cough.

Secretomotor fibers supply the mucous glands.

Sympathetic supply to the lungs is from T2 to T5 segments.

They are inhibitory to the smooth muscle and glands.

2. *Bronchopulmonary Segments*

Bronchopulmonary segments are well-defined sectors of the lung, each one of which is aerated by a segmental bronchus. Each segment is pyramidal in shape with its apex directed towards the root of the lung.

There are 10 segments on the right side and 8 segments on the left.

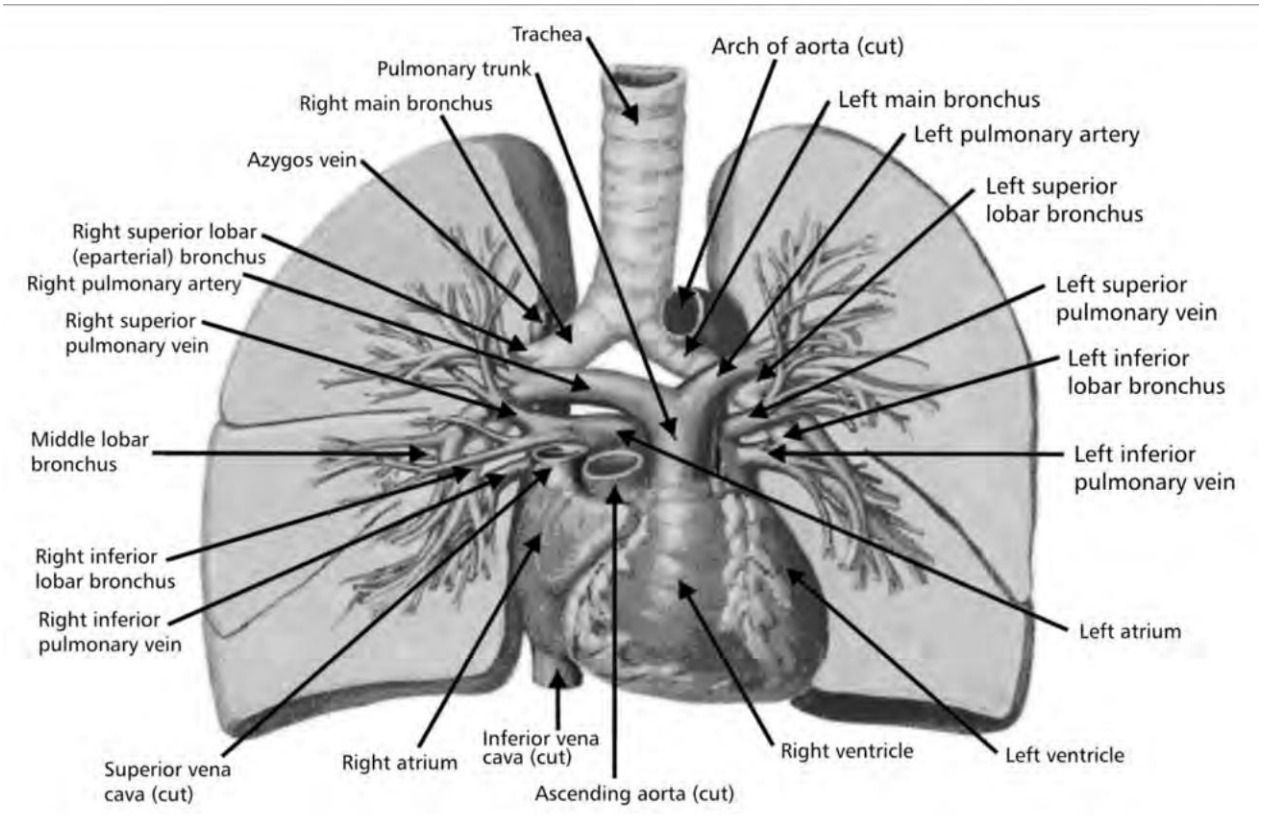


Fig. 8.12 *Pulmonary arteries and veins*

3. Applied Anatomy

1. Usually infection of a segment remains restricted to it; although some infections (e.g., tuberculosis) may spread from one segment to another.
2. Segments are no barriers to the spread of bronchogenic carcinoma.
3. Knowledge of the detailed anatomy helps considerably in the following:
   - Surgical removal of a segment
   - Postural drainage

   In postural drainage, draining of infection is done by making the patient adopt a particular posture so that the affected segment assumes a higher level of position; thus, due to gravity and coughing, sputum and secretions are drained downwards and are then coughed out.
4. **Bronchoscopy** is a procedure in which visualizing the interior of the bronchi is made possible by passing an instrument, bronchoscope, through the mouth and trachea.

8.1.8 Mediastinum

The mediastinum is the 'middle' section of the chest cavity. The chest cavity contains the right and left lungs, which lie on either side of the heart. The mediastinum is bordered by the thoracic inlet (where the organs of the neck enter/leave the chest) on the upper side, by the diaphragm on the lower side, the sternum in front, and the vertebral column on the back.

The mediastinum is artificially divided into the anterior, middle, and posterior and superior regions. It contains all of

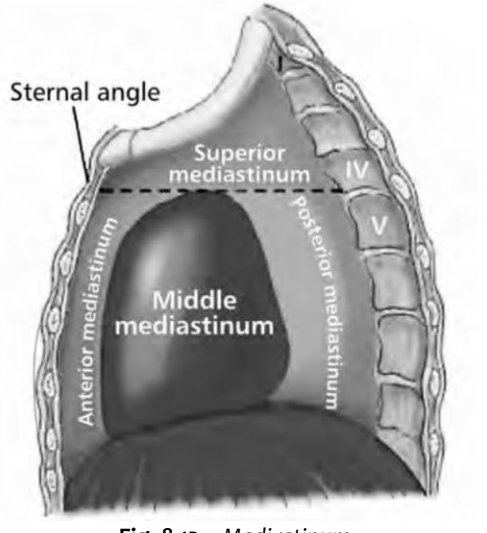


Fig. 8.13 *Mediastinum*

the chest organs except the lungs. Organs located in the mediastinum include the heart, the aorta, and the thymus gland, the thoracic portion of the trachea, the esophagus, lymph nodes and important nerves.

8.1.9 Pleura and Pleural Cavity

The lung invaginates into the pleura. The pleura has 2 layers made of serous membrane. Between the two layers there is a small amount of serous fluid.

- The **visceral pleura** is adherent to the lung and also passes into the fissures.
- The **parietal pleura** is adherent to the inner side of the thoracic wall and diaphragm.

The parietal pleura is continuous with the visceral pleura at the hilum.

The pleural cavity is a potential space. The serous fluid in it prevents friction between the two layers and helps them glide over each other. Because of the surface tension between them, they cannot be easily separated.

If any one layer is punctured, the underlying lung collapses.

Applied Anatomy

1 Diseases of the lung, e.g., pneumonia, tuberculosis may invade the pleura causing pleurisy. It may be dry (dry pleurisy) or fluid may accumulate in the pleural cavity (pleural effusion).
2 Fluid may collect in the pleural cavity (hydrothorax) as a part of generalized edema.

8.1.10 Pulmonary Circulation

Discussed in the chapter on cardiovascular system

8.2 PHYSIOLOGY

8.2.1 Mechanism of Respiration

Inspiration is an active process and expiration is a passive process.

The respiratory cycle occurs 14 to 16 times a minute and consists of 3 phases:

- Inspiration
- Expiration
- Pause

The thoracic cage is the structure formed by the thoracic vertebrae, ribs, the sternum and the costal cartilages that attach the ribs to the sternum. There is enlargement of the thoracic cage and expansion of lungs during inspiration; while during expiration, the thoracic cage and lungs decrease in size and come back to the pre-inspiratory position. The role of the thoracic cage in the process of respiration is discussed elsewhere.

1. Diaphragm

The diaphragm is the primary muscle of inspiration. It is a thin, dome-shaped structure separating the thoracic and abdominal cavities. It is attached to the lower ribs and it forms the floor of the thoracic cavity and the roof of the abdominal cavity. It consists of a central tendon and its fibers are attached to the sternum, the ribs and the vertebral column.

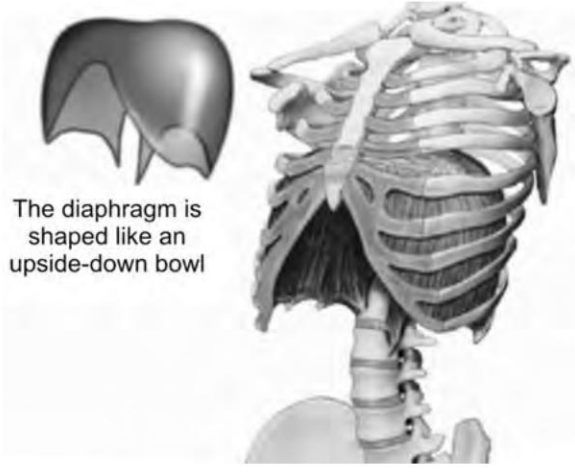


Fig. 8.14 *Diaphragm*

When it contracts, it pushes downward and enlarges the thoracic cavity in length. The thoracic-cavity pressure is decreased. It pushes the abdominal cavity and there is increase in pressure in the abdominal cavity and the contents are pushed down and out.

Also, as the diaphragm is covered by the inferior surface of the parietal pleura, it pulls the pleura with it. Thus the pleural pressure is lowered. This causes the alveolar pressure to drop and air flows into the lungs. During quiet expiration, the diaphragm passively relaxes and returns to its original position.

The intercostal muscles and diaphragm work together and contract simultaneously, thus leading to enlargement of the thoracic cage in all the sides—antero posteriorly, side to side and top to bottom.

During quiet breathing, the diaphragm moves a centimeter or two up and down, but during exercise, it can move more than 10 cm. This increases the abdominal pressure more than usual.

The diaphragm is supplied by the phrenic nerve from 3rd, 4th, and 5th cervical segments.

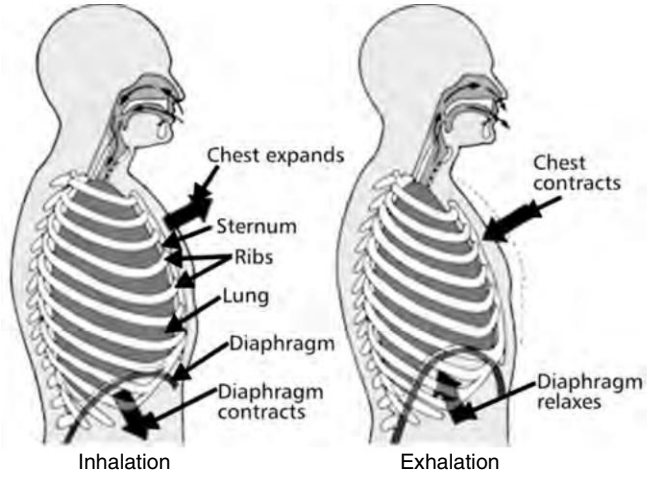


Fig. 8.15 *Mechanism of breathing*

2. Muscles of Respiration

Muscles of respiration are of 2 types:

- Inspiratory muscles
- Expiratory muscles

Inspiratory muscles are of two types—primary and accessory.

Expiratory muscles are also of two types—primary and accessory.

Primary inspiratory muscles are

- Diaphragm (discussed above), supplied by the phrenic nerve
- Intercostal muscles, supplied by intercostal nerves

Accessory inspiratory muscles are

- Sternomastoid,
- Scalene,
- Serratus anterior,
- Elevators of scapulae, and pectoralis.

Primary expiratory muscles are intercostal muscles.

Accessory expiratory muscles are abdominal muscles.

During normal quiet breathing, the primary muscles are involved in the change in size of thoracic cage.

During forced respiration, the accessory muscles help the primary muscles.

3. Movements of the Lungs

(a) Inspiration Inspiration causes enlargement of thoracic cage in all the diameters. This is due to elevation of ribs and descent of diaphragm.

Change in the size of thoracic cavity occurs because of the movements of certain structures, viz., thoracic lid, diaphragm, the ribs, the intercostal muscles and the sternum.

The visceral pleura is adherent to the lungs and the parietal pleura is adherent to the inner wall of the thorax and to the diaphragm.

The capacity of the thoracic cavity is increased by simultaneous contraction of intercostal muscles and the diaphragm. The parietal pleura moves with the walls of the thorax and diaphragm. The pressure in the pleural cavity is thus reduced to a level much lower than the atmospheric pressure. The visceral pleura follows the parietal pleura and pulls the lung with it.

The lungs are thus stretched and pressure within the alveoli and the air passages falls. Air is drawn into the lungs in an attempt to equalize the atmospheric and alveolar air pressures.

The process of inspiration is active as it requires expenditure of energy for muscle contraction.

(b) Expiration There is relaxation of intercostal muscles and the diaphragm. So, there is upward and inward movement of the thoracic cage. There is elastic recoil of the lungs. Pressure inside the lungs exceeds that in the atmosphere. Air is expelled from the respiratory tract. This is expiration. Some air will always be in the lungs and this prevents collapse of the lungs. Collapse of the lungs is also prevented by the intact pleura.

The process of expiration is a passive process as it does not require expenditure of energy.

After expiration, there is a pause and then the next cycle begins.

4. Factors Affecting Normal Respiration

There are certain factors which affect normal respiration. They are as follows:

(a) Elasticity Elasticity is the ability of the lung to return to its normal shape after each breath. When there is loss of elasticity of the connective tissue of the lungs then increased effort is required for inspiration. Expiration is also forced.

(b) Compliance Compliance is the measure of the distensibility of the lungs. It gives the measure of the effort required to inflate the alveoli. When compliance is low, the effort needed to inflate the lungs is more than normal.

(c) Resistance to Air Flow When resistance to air flow is increased, more effort is required to inflate the lungs, e.g., due to spasm of the bronchi.

8.2.2 Regulation of Respiration

Normal respiration in a healthy adult is 14 to 18 times per minute with an average tidal volume of 500 mL. Voluntary control of respiration is possible only for a short period of time. One can hold the breath for a longer period if one practices, but, ultimately the person has to breathe.

Respiration changes under certain conditions. Anxiety, exercise or emotional stress increases the rate and depth of

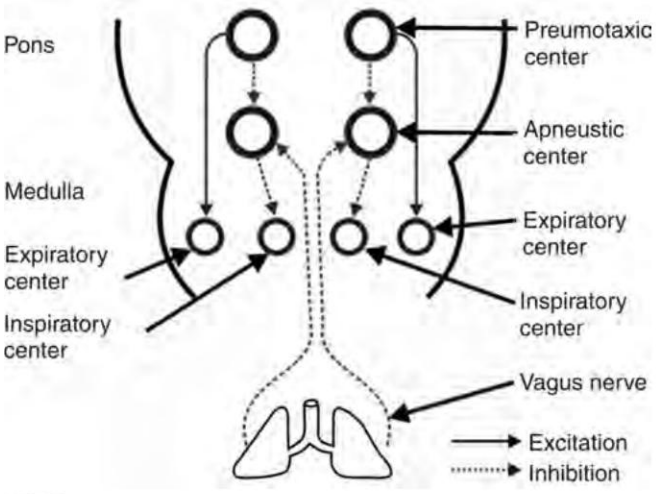


Fig. 8.16 *Organisation of respiratory centers (Refer colour figure)*

respiration. There are certain regulatory mechanisms which help bring back the respiration to normal.

There are two main mechanisms of respiratory control:

1. Nervous control
2. Chemical control

1. Nervous Mechanism

Respiratory Centre Continuous exchange of gases between alveoli and blood makes it possible for proper supply of oxygen to the tissues. Simultaneously, carbon dioxide is removed from the tissues.

The respiratory center controls respiratory movements, which is responsible for alveolar ventilation. This alveolar ventilation is necessary for gaseous exchange.

The respiratory center is composed of several groups of nerve cells that control the rate and depth of respiration. They are located bilaterally in the medulla oblongata and pons.

The respiratory center is divided into three major groups:

- A **dorsal** respiratory group located in the dorsal portion of the medulla, which mainly causes inspiration.
- A **ventral** respiratory group located in the ventrolateral part of the medulla, which can cause either expiration or inspiration, depending on which neurons are stimulated.
- Neurons in the **pneumotaxic** and **apneustic** centers are situated in the pons. They influence the dorsal (inspiratory) and ventral (expiratory) neurons of the medulla.

Motor impulses leaving the respiratory centre pass in the phrenic and intercostal nerves.

The phrenic nerve supplies the diaphragm and intercostal nerves supply the intercostal muscles.

Signals from the inspiratory center are sent slowly, which brings the onset of inspiration and these impulses steadily increase but abruptly cease.

This leads to smooth inspiration with steady increase in volume of air in the lung alveoli.

Expiratory centers are inactive during quiet breathing. When respiratory rate increases, e.g., during stress, some impulses from the inspiratory center spill over to the expiratory center and they start sending signals to motor neurons of inspiratory muscles and help inspiration.

Thus, the expiratory center helps both the process of inspiration and expiration but not during quiet breathing.

2. Chemical Mechanism

Chemoreceptors **Chemoreceptors** are located centrally and peripherally which respond to changes in the partial pressure of O_2 and CO_2 in the blood and cerebrospinal fluid.

Three factors stimulate respiration in order to maintain pO_2 (plasma O_2 concentration), pCO_2 (plasma CO_2 concentration) and pH (H-ion concentration) of the blood. The mechanism by which these factors affect respiration is known as 'chemical control of respiration'.

The factors affecting respiration are

1. O_2 lack, i.e., fall of pO_2 (hypoxia)
2. CO_2 excess, i.e., increase in pCO_2 (hypercapnia)
3. Increase in H-ion concentration or decrease in pH- (alkalosis or acidosis).

There are two types of chemoreceptors:

1. Central chemoreceptors
2. Peripheral chemoreceptors

Central Chemoreceptors Central chemoreceptors are present on the surface of the medulla oblongata, lie in close contact with blood and are bathed in cerebrospinal fluid.

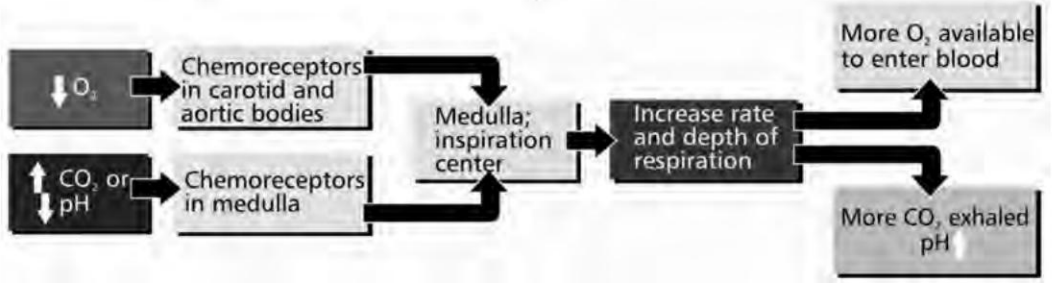


Fig. 8.17 *Chemical regulation of respiration*

When arterial pCO_2 rises even slightly, the central chemoreceptors are stimulated. The respiratory center–inspiratory center is stimulated and there is increase in the rate and force of respiration. Ventilation of the lungs is increased and arterial pCO_2 is decreased.

The sensitivity of the central chemoreceptors to raised arterial pCO_2 is the most important factor in maintaining homeostasis of blood. A small reduction in pO_2 has less effect, but a marked reduction has a depressing effect.

Peripheral Chemoreceptors Peripheral chemoreceptors are situated in the arch of the aorta and in the carotid bodies. They are more sensitive to small rises in arterial pCO_2 than to similarly low arterial pO_2 levels. The chemoreceptors are stimulated and impulses go via the vagus and glossopharyngeal nerves to the respiratory center, the rate and depth of respiration increases and brings the level of oxygen and carbon dioxide to normal.

Homeostasis is maintained by normal quiet breathing. Thus, effective control of respiration enables the body to maintain homeostasis of blood gases during various changes in physiological, environmental and pathological conditions.

8.2.3 Respiratory Reflexes

1. Hering–Breuer Reflex

Stretch receptors are situated on the wall of bronchi and bronchioles of lungs. They respond to stretching of lung tissue.

When the lungs expand, and are inflated, the stretch receptors are stimulated and send impulses to the respiratory center via the vagus nerve. The inspiratory center is inhibited and inspiration stops and expiration starts.

There is restriction of inspiration and, thus, this reflex prevents over-inflation of the lungs. It is actually a protective reflex. This is called Hering–Breuer reflex. This reflex does not operate during normal quiet breathing.

2. Impulses from 'J' Receptors of Lungs

'J' receptors are juxtacapillary receptors, which are found on the walls of the alveoli. They are in close proximity with the pulmonary capillaries.

Stimulation of these receptors produces a response leading to apnoea (cessation or stoppage of breathing) which is followed by hyperventilation, bradycardia, hypotension and skeletal-muscle weakness.

The exact role of the 'J' receptors is not very clear. In patients with pulmonary congestion and left cardiac failure, the 'J' receptors bring about hyperventilation.

(a) Role of Baroreceptors Baroreceptors are situated in the carotid sinus and arch of the aorta.

They are activated whenever there is increase in arterial blood pressure. Impulses go to the medulla and respiration is inhibited.

(b) Impulses from Irritant Receptors of Lungs or Pulmonary Irritant Reflex Irritant receptors are situated in the wall of the bronchi and bronchioles of lungs. Harmful chemical agents like ammonia stimulate these receptors, which in turn send impulses to the respiratory center via the vagus nerve. There is reflex hyperventilation and bronchospasm. The harmful irritants are prevented from entering the lungs.

(c) Response to Pain Whenever there is pain, impulses are sent to the cerebral cortex, which in turn send impulses to the respiratory center and there is hyperventilation.

(d) Cough and Sneeze Reflexes They are both protective reflexes.

In cough reflex, when larynx or trachea are irritated, impulses go via the vagus nerve and cough occurs. There is deep inspiration followed by deep expiration and as intrapleural pressure rises, the glottis opens and the irritant is expelled.

During sneezing, the olfactory receptors and trigeminal nerve endings are stimulated by an irritant and there is deep inspiration followed by forceful effort of the glottis and the irritant gets expelled.

Breathing may change due to impulses from the brain and higher centers. Emotional changes, fear, anxiety, talking and singing can cause hyperventilation.

Temperature influences the rate and depth of respiration.

8.2.4 Principles of Gas Exchange

Respiration occurs in four stages:

- **Ventilation,** i.e., movement of air into and out of the alveoli of the lungs.
- **Pulmonary gas exchange,** i.e., exchange of gases between the alveoli and pulmonary capillaries.
- **Transport of gases** from the pulmonary capillaries through the circulation to the periphery and back to the lungs along the circulation.
- **Peripheral gas exchange**, i.e., exchange of gases between the tissue capillaries and the tissues and impacting the cells and mitochondria within the cells.

Oxygen and carbon dioxide are transported from the lungs to the tissues and from tissues to the lungs. Gases diffuse from a level of higher concentration to a level of lower concentration across a semipermeable membrane till equilibrium is reached on both the sides. According to this principle, there is exchange of gases, both in the lungs and in the tissues.

1. External Respiration

External respiration means exchange of gases by diffusion between the alveoli and the blood. There is a network of tiny

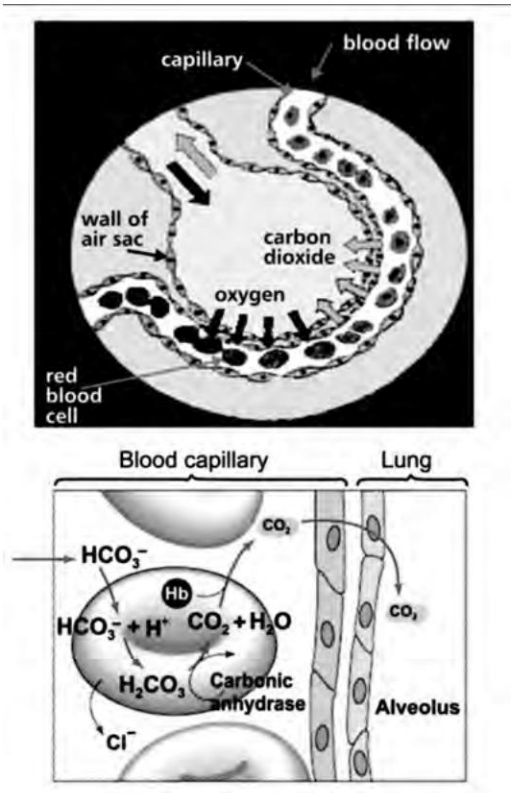


Fig. 8.18 *External respiration (Refer colour figure)*

capillaries surrounding each alveolar wall. The total surface area for gas exchange in the lungs is 60 to 70 square meters.

The respiratory membrane plays a very important role in the exchange of respiratory gases. It is formed by the epithelium of the respiratory unit and the endothelium of the pulmonary capillaries.

The capillaries are in close contact with the epithelium of the respiratory unit. The alveolar gases are close to the blood in the capillaries. This allows easy gaseous exchange between air in the alveoli and blood in the capillaries.

Inspired air has a pO_2 of 158.2 mmHg and pCO_2 is 0.3 mmHg. The blood coming from the heart to the lungs through the pulmonary arteries has a pO_2 of 40.0 mmHg and pCO_2 of 46.0 mmHg. Due to this difference in the partial pressure, O_2 diffuses from alveoli into the blood. CO_2 diffuses from venous blood into the alveoli as venous blood has a high level of CO_2 and low level of O_2, since it has returned from the tissues. The flow of blood through the capillaries is slow, which increases the time available for diffusion to take place. In the atmospheric air, the partial pressure of carbon dioxide is very insignificant and only 0.3 mmHg, while in the alveoli it is 40.0 mmHg. So, carbon dioxide easily goes to the atmosphere. Hence, now the oxygen and carbon dioxide concentration in the blood leaving the alveolar capillaries are in equilibrium with those of alveolar air. The blood going from the lungs to the heart has a pO_2 of 100 mmHg and pCO_2 as 40.0 mmHg.

2. Internal Respiration

Internal respiration means the exchange of gases by diffusion between blood in the capillaries and the body cells.

Blood arriving at the tissues is saturated with O_2. This blood has come from the lungs and so has a higher pO_2 and a lower pCO_2 than the tissues. pO_2 is 40.0 mmHg in the tissues and 100.0 mmHg in the arterial blood. pCO_2 is 46.0 mmHg in the tissues and 40.0 mmHg in the arterial blood. Hence, gaseous exchange takes place as there is a concentration-gradient between the blood and the tissues. O_2 diffuses through the capillary wall into the tissues and enters the cell. CO_2 diffuses from the cells into the extracellular fluid. From here it passes into the blood of the capillaries. The pO_2 is now about 40.0 mmHg and pCO_2 is 46.0 mmHg in the blood which then goes to the lungs and the cycle goes on.

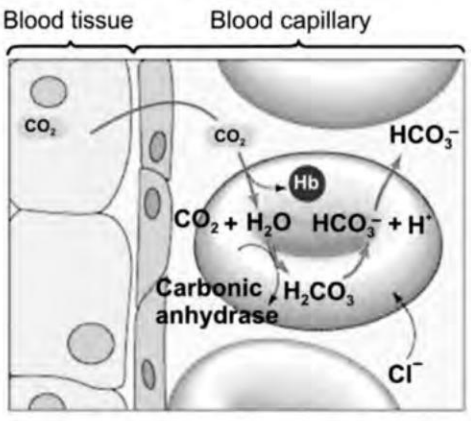


Fig. 8.19 *Internal respiration (Refer colour figure)*

3. Transport of Oxygen in the Bloodstream

Transport of blood O_2 and CO_2 is necessary for internal respiration to occur.

98% of the blood that enters the left atrium from the lungs has passed through the alveolar capillaries and has become oxygenated.

Oxygen is carried in the blood as oxyhemoglobin, i.e., oxygen combines with hemoglobin. 98.5% of blood O_2 is carried in this form.

The rest 1.5% of blood O_2 is dissolved in plasma fluid.

Oxyhemoglobin is an unstable compound. It is only a physical combination. This is useful, because whenever needed, it is readily released. It dissociates releasing O_2 under certain conditions like

- Raised CO_2 content of tissue fluid
- Raised temperature
- Raised 2, 3-diphosphoglycerate.

When tissues are more active, there is increased production of CO_2 and heat. Increased O_2 is released, and O_2 diffuses from the capillary into the extracellular fluid. O_2 then diffuses

rapidly from extracellular fluid into the cell. Only 3 mmHg of O_2 pressure is required for full support of metabolic process of cell.

When pO_2 is 40.6 mmHg, it quickly loses oxygen. If, pO_2 is above 80 mmHg, it means that saturation is of hemoglobin with O_2 as 100%. No loading of O_2 is now possible.

This relationship of saturation of hemoglobin with O_2 can be shown by a curve called the **oxygen dissociation curve**. This curve shifts to the left when temperature decreases or pCO_2 decreases or there is increase in pH. This is called **Bohr's effect**.

Oxygen dissolved in plasma is in very small measure but still important in certain situations, e.g., during strenuous exercise, there is more demand for O_2, which is met with by this plasma-dissolved O_2.

Normally, rate of O_2 utilized by the cells is controlled by rate of energy expenditure in the cells.

Factors Affecting Intracellular Fluid pO_2 Increased rate of blood flow will increase the pO_2 of intracellular fluid and greater quantity of O_2 is transmitted to tissue.

Increased rate of O_2 utilization by tissues will decrease the pO_2 of intracellular fluid.

If hemoglobin content of blood is decreased, there is fall in intracellular fluid pO_2.

4. Transport of Carbon Dioxide in the Bloodstream

Principle of CO_2 carriage is the same as that of O_2 carriage, i.e., passive diffusion.

Diffusion of CO_2 is in a direction exactly opposite to that of the diffusion of O_2, but there is one major difference between these two diffusions; CO_2 diffuses about 20 times as rapidly as O_2.

So pressure difference which causes CO_2 diffusion is much less than the pressure difference which causes O_2 diffusion.

CO_2 is transported by three mechanisms.

1. Most of the CO_2 is in the form of bicarbonate ions in the plasma. 70% of blood CO_2 is transported in this way.
2. Some of the CO_2 is dissolved in the plasma. 7% of blood CO_2 is in this form.
3. Some of the CO_2 is carried in erythrocytes loosely combined with hemoglobin as carbimino hemoglobin. 23% of blood CO_2 is in this form.

CO_2 diffuses out of the tissue cell. After entering into the blood, it is transported to lungs.

On arriving at the lungs, CO_2 is rapidly transferred from the capillary blood to the alveoli because of 20 times greater diffusion coefficient of CO_2.

As CO_2 diffuses out of the capillary blood, low CO_2 tension increases the uptake of O_2 from the alveoli. Thus, CO_2 is liberated.

5. Chloride Shift

When CO_2 enters the blood, chloride ions enter the red blood cells from the plasma and sodium remains as it is. When CO_2 leaves the blood, chloride ions come out of the cells and once again combine with sodium. This is called chloride shift.

The membrane of red blood cells is permeable to Cl^- and HCO_3. It is not permeable to Na^+ and K^+. CO_2 forms H_2CO_3 when it enters the blood. This is in the presence of an enzyme, **carbonic anhydrase**. This reacts with $KHbO_2$ and O_2 is liberated. O_2 passes from the blood into the tissues.

Hemoglobin is reduced to HHb. K^+ and HCO_3^- are formed. HCO_3^- comes out of the plasma and combines with NaCl to form $NaHCO_3$ and Cl gets liberated. This moves to the red blood cells to combine with K^+ to form KCl.

In the alveoli, O_2 enters the blood to combine with reduced Hb to form $HHbO_2$. This reacts with KCl to form $KHb+O_2$, and H^+ and Cl^- are released. Cl^- moves towards plasma where it reacts with $NaHCO_3$, forms NaCl and releases HCO_3, which diffuses into the red blood cells to form H_2CO_3 with H^+ ions. This now dissociates into CO_2 and H_2O which diffuse out and go into the atmosphere.

Each 100 mL of blood passing through the lungs liberates 4 mL of CO_2.

8.2.5 Pulmonary Volumes

Ventilation is the process by which atmospheric air is drawn into the lung alveoli, which is called inspiration, and alveolar air is exhaled out into the atmospheric air, which is called expiration.

Ventilation depends on the following factors:

- Patency of the respiratory passage
- Healthiness of the lung tissues
- Unrestricted movement of thoracic cage
- Neuromuscular control

Ventilation has three main aspects:

1. Pulmonary volumes (lung volume)
2. Pulmonary capacities
3. Mechanism of breathing

1. Lung Volumes

Lung volume means the volume of air present in the lung at different stages of respiration.

During normal quiet breathing, there are about 15 respiratory cycles per minute. The exchange of gases takes place only across the walls of alveolar ducts and alveoli. The remaining capacity of the respiratory passages is called anatomical dead space, and the air present here is about 150 mL.

There are four lung volumes:

1. Tidal volume (TV)
2. Inspiratory reserve volume (IRV)

3. Expiratory reserve volume (ERV)
4. Residual volume (RV)

(a) Tidal Volume (TV) Tidal volume means the amount of air which passes into and out of the lungs during one cycle of quiet breathing. It is 500 mL. Tidal volume signifies the normal depth of breathing.

(b) Inspiratory Reserve Volume (IRV) Inspiratory reserve volume is the extra volume of air that can be inhaled into the lungs forcefully with maximal effort. It is 3300 mL.

(c) Expiratory Reserve Volume (ERV) Expiratory reserve volume is the additional volume of air which can be expelled from the lungs after normal expiration with maximal effort. It is 1000 mL.

(d) Residual Volume (RV) Residual volume is the volume of air remaining in the lungs after forced expiration. It is 1200 mL.

2. *Measurement of Lung Volumes*

Lung volume can be determined by a spirometer.

There are two types of spirometers:

1. Inspiratory spirometer
2. Expiratory spirometer

Inspiratory spirometer measures

1. Tidal volume
2. Inspiratory reserve volume

Expiratory spirometer can measure

1. Tidal volume
2. Expiratory reserve volume
3. Vital capacity. (See Fig. 8.20)

3. *Pulmonary Capacities*

Whenever two lung volumes are added or when a single lung volume is expressed in terms of time, it is known as pulmonary capacity or ventilatory capacity.

There are four lung capacities

1. Inspiratory capacity
2. Functional residual capacity
3. Total lung capacity
4. Vital capacity

(a) Inspiratory Capacity (IC) Inspiratory capacity is the maximum amount of air that can be inhaled after the end of expiration.

It is the sum of tidal volume and inspiratory reserve volume.

Tidal volume + inspiratory reserve volume = inspiratory capacity

TV + IRV = IC

500 mL + 3300 mL = 3800 mL

(b) Functional Residual Capacity (FRC) Functional residual capacity is the amount of air remaining in the air passages and alveoli at the end of expiration.

It is the sum of expiratory reserve volume and residual volume.

Expiratory reserve volume + residual volume = functional residual capacity

ERV + RV = FRC

1000 mL + 1200 mL = 2200 mL

Functional residual capacity prevents collapse of alveoli after expiration.

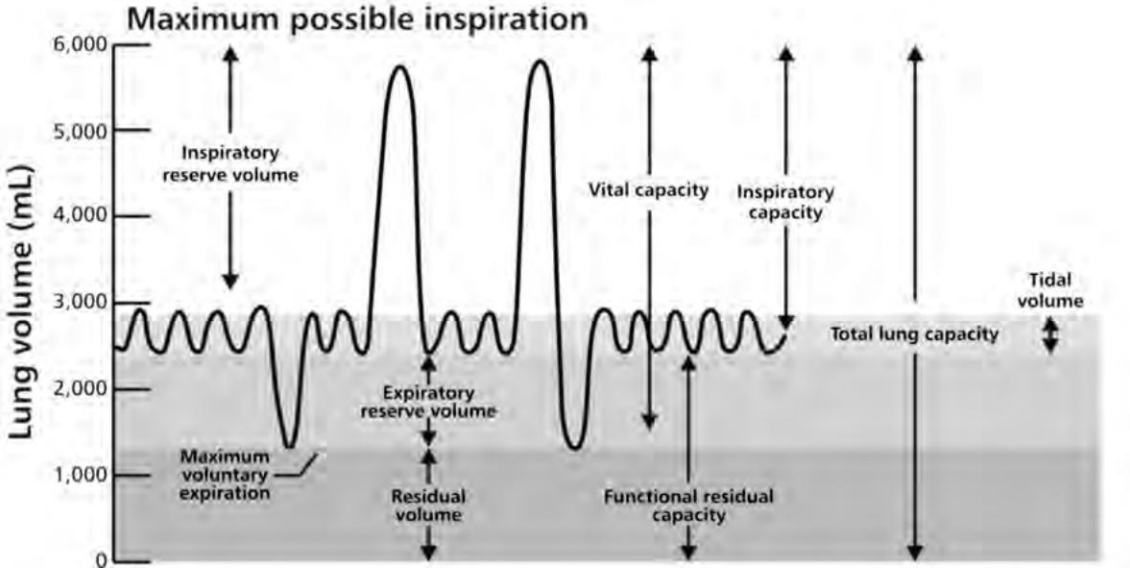


Fig. 8.20 *Lung volumes and capacities*

(c) Total Lung Capacity (TLC) Total lung capacity is the amount of air present in the lungs after a maximal inspiration.

It is the sum of tidal volume + inspiratory reserve volume + expiratory reserve volume + residual volume.

TV + IRV + ERV + RV = TLC
500 mL + 3300 mL + 1000 mL + 1200 mL = 6000 mL

(d) Vital Capacity (VC) Vital capacity is the maximum volume of air which can be forcefully expelled after maximum inspiration. In other words, it is the maximum volume of air which can enter and leave the lungs.

It is the sum of tidal volume + inspiratory reserve volume + expiratory reserve volume

TV + IRV + ERV = VC
3300 mL + 500 mL + 1000 mL = 4800 mL

Physiological Variations

1. Vital capacity is less in females than in males.
2. Vital capacity is more in heavily built persons.
3. Vital capacity is decreased in persons doing sedentary jobs. Persons who play musical instruments, e.g., the saxophone, have more vital capacity.
4. Vital capacity is more in standing and less in the lying position.
5. Vital capacity is more in athletes.

Pathological Variations Vital capacity gets greatly reduced in persons suffering from asthma, emphysema, pneumonia, congestion of lungs, weakness or paralysis of respiratory muscles, pneumothorax, hemothorax, hydrothorax, pyothorax, pulmonary edema and pulmonary tuberculosis.

(e) Forced Expiratory Volume (FEV) Forced expiratory volume is defined as the amount of air which can be expired forcefully after taking a deep breath. The forced expiratory volume in the first second is FEV1. FEV1 is by far the most frequently used index for assessing airway obstruction, bronchoconstriction or broncodilatation. It is expressed as a percentage of the vital capacity.

(f) Alveolar Ventilation Alveolar ventilation is the volume of air that moves into and out of the alveoli (lungs) per minute. It is the volume of air that takes part in gaseous exchange, which is equal to the tidal volume minus the anatomical dead space, multiplied by the respiratory rate/minute.

AV = (TV – anatomical dead space) × RR
= (500 – 150) mL × 15/min
= 5.25 liters per minute

Increased rate of O_2 utilization by tissues will decrease the pO_2 of intracellular fluid.

If hemoglobin content of blood is decreased, there is fall in intracellular fluid pO_2.

8.2.6 Pulmonary Function Tests

Pulmonary function tests are a group of tests that measure how well the lungs breathe in and breathe out the air and how well they move oxygen into the blood.

Lung volumes and capacities are measured using an instrument called **spirometer**.The modified spirometer is called **respirometer** and the method is called spirometry.

Spirometry

In a spirometry test, the person breathes into a mouthpiece that is connected to an instrument called a spirometer. The spirometer records the amount and the rate of air that the person breathes in and out over a period of time.

For some of the test measurements, one can breathe normally and quietly, while other tests require forced inhalation or exhalation after a deep breath.

The patient should not eat a heavy meal before the test. If he is a smoker he should not smoke for 4–6 hours before the test. Specific instructions will be given whether to stop using bronchodilators or inhaler medications. It may become necessary to breathe in medication before the test.

Since the test involves some forced breathing and rapid breathing, there may be some temporary shortness of breath or light-headedness during and after the test, for some period of time. One has to breathe through a tight-fitting mouthpiece, and the nose will be clipped.

Indications

- To diagnose certain types of lung disease (especially asthma, bronchitis, and emphysema)
- To find the cause of shortness of breath
- To see if exposure to contaminants, at work, affects lung function
- To assess the patient pre-operatively
- To assess the effect of medication
- To measure progress in disease treatment

Spirometry measures air flow, by measuring how much and how quickly you exhale. Lung volume measures the amount of air in the lungs without forcibly blowing out. In some lung diseases (such as emphysema and chronic bronchitis), the lungs contain too much air; while in other lung diseases, such as fibrosis of the lung, the lungs get scarred and smaller so that they contain too little air.

Normal values are based upon age, height, ethnicity, and sex. Normal results are expressed as a percentage. A value is usually considered abnormal if it is less than 80% of the predicted value.

Fig. 8.21 *Spirometry measures how fast and how much air you breathe out*

Abnormal results usually mean that the patient may have some chest or lung disease.

The risk of this test is minimal for most of the people. There is a small risk of collapsed lung in people with a certain type of lung disease. The test should not be given to a person who has experienced a recent heart attack, or who has certain other types of heart disease.

The cooperation of the patient while performing the test is crucial in order to get accurate results. A poor seal around the mouthpiece of the spirometer can give poor results.

Residual volume and functional residual capacity cannot be measured by a spirometer, so other indirect methods are used to measure them.

There are two methods for measuring residual volume and functional residual capacity:

- Helium dilution technique
- Nitrogen wash-out method

(a) Helium Dilution Technique

Procedure This technique is a closed-circuit system. The respirometer is filled with a mixture of air and a known quantity of helium. In the beginning, the subject breathes normally. Then the subject is asked to breathe from the respirometer at the end of expiration. The helium from the respirometer enters the lungs and starts mixing with the air in the lungs. After a few minutes of breathing, concentration of helium in the respirator becomes equal to concentration of helium in the lungs. As there is no leak, the amount of helium remains constant throughout the test. The amount of helium in the respirator is determined.

From the formula, the functional residual capacity can be measured.

$$\text{FRC} = V\frac{(C_1 - C_2)}{C_2}$$

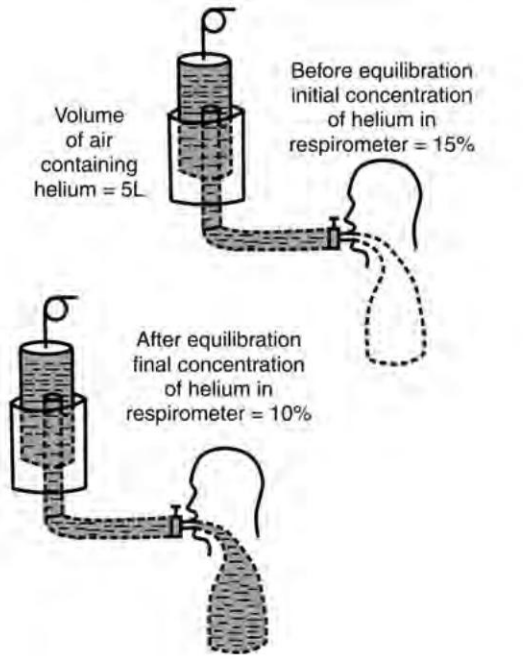


Fig. 8.22 *Helium dilution technique*

where

C_1 = Initial concentration of helium in respirometer

C_2 = Final concentration of helium in respirometer

V = Initial volume of air in respirometer

In measuring the functional residual capacity, the subject starts breathing after the end of normal expiration while in measuring residual volume, the subject starts breathing from the respirometer after forced expiration.

(b) Nitrogen Wash-out Method Normal concentration of N_2 in air is 80%. If the total quantity of nitrogen in the lungs is measured the amount of air in the lungs can be calculated.

Procedure The subject breathes normally and inspires pure O_2 through a valve and expires into a Douglas bag. This is carried out for 6 to 7 minutes till N_2 in the lungs is replaced by O_2. N_2 comes into the Douglas bag.

The following are measured:

- Volume of air collected in the Douglas bag
- Concentration of N_2 in the Douglas bag

$$\text{FRC} = \frac{C_1 \times V}{C_2}$$

where

C_1 = Concentration of N_2 in the collected air

C_2 = Normal concentration of N_2 in air

V = Volume of air collected

In measuring the functional residual capacity, the subject starts inhaling pure O_2 after the end of normal expiration; and

in measuring the residual volume, the subject starts breathing pure O_2 after forceful expiration.

Both methods are equally reliable and safe when measuring the FRC of patients on mechanical ventilation but the nitrogen method is easier and quicker.

8.3 ARTIFICIAL RESPIRATION

Artificial Respiration (AR) is required whenever there is stoppage or failure of breathing without cardiac arrest.

Artificial respiration is necessary in the following situations:

- Drowning
- Poisoning from gases
- Deep anesthesia
- Accidents
- Electric shock

8.3.1 Purpose of Artificial Respiration

The purpose of artificial respiration is to ventilate the alveoli and to stimulate the respiratory centers.

Brain tissue is affected by irreversible changes if oxygen is not supplied to it for more than 3 minutes. Resuscitation must be started immediately in the form of artificial respiration before the heart stops.

8.3.2 Methods

Artificial respiration is carried out by two methods:

1. Manual methods
2. Mechanical methods

1. Manual Methods

Manual methods can be immediately carried out.

The main purpose of this method is to provide clear air. Usually, when there is an accident, people always crowd in. People should be asked to move away from the affected person, so that he gets fresh air. Clothes around the chest and neck are loosened. The mouth and throat should be cleared of mucous, saliva and foreign particles. If there is a denture, it should be removed. The tongue is drawn forward and prevented from falling back so that the airway is not obstructed.

There are 2 manual methods:

(a) Mouth-to-mouth method
(b) Holger–Nielsen method

(a) Mouth-to-mouth Method The subject is placed in a supine position, and the resuscitator kneels at the side of the subject.

Thumb of the resuscitator is kept on the subject's mouth and the lower jaw is pulled downwards.

The nostrils of the subject are closed with the thumb and index finger of the other hand of the resuscitator.

The resuscitator then takes a deep breath and exhales air into the subject's airway which expands the lungs. The volume of air exhaled must be twice the normal tidal volume.

The resuscitator removes his mouth and a passive expiration occurs in the subject due to elastic recoil of the lungs.

This procedure should be repeated 12 to 16 times a minute, till normal respiration is restored.

The advantage of this method is that CO_2 in the expired air, which has been pushed into the subject from the resuscitator, can directly stimulate the respiratory center and facilitate onset of normal respiration.

The disadvantage is that there is a close contact between the mouths of the resuscitator and the subject and this could lead to spread of infection from resuscitator to subject and vice versa.

(b) Holger–Nielsen Method or Back-pressure Arm-lift Method The subject is placed in a prone position with his head on one side. The hands of the subject are placed under the cheeks. Elbows are flexed and shoulders are kept abducted. The resuscitator kneels beside the subject. He puts his hands on the back of the subject and spreads out his fingers. Then he pushes on the back of the subject without flexing his elbows.

The weight of resuscitator and the pressure exerted by him causes air to be expelled from the lungs. Then the resuscitator takes himself off the patient's back. The pressure is released. Simultaneously, the subject's arms are drawn forward. This results in expansion of the thoracic cage and air flows into the lungs.

This procedure is carried out 12 to 16 times a minute till normal respiration is restored.

2. Mechanical Methods

When respiratory failure is due to paralysis of respiratory muscles or when manual methods are not useful, mechanical methods are used, as here artificial respiration is needed for a longer time.

There are two mechanical methods:

(a) Drinker's method
(b) Ventilation method

(a) Drinker's Method Here, an iron lung chamber or tank respirator is used. It has an airtight chamber of iron or steel. The patient is placed in the chamber but the head is kept outside.

Using pumps, pressure inside the chamber is made positive and negative alternately.

When there is negative pressure in the chamber, the subject's thoracic cage expands and inspiration occurs; and when

Fig. 8.23 *Process of mouth-to-mouth resuscitation*

there is positive pressure in the chamber, expiration occurs.

The patient can get the advantage of artificial respiration for a longer time with this machine.

(b) Ventilation Method A rubber tube is introduced into the trachea through the mouth. Air or O_2 is pumped into the lungs with intermittent pressure. The lungs inflate. When pumping of air is stopped, expiration occurs. The cycle is repeated.

The apparatus used here is a ventilator. They are of two types:

- Volume ventilator
- Pressure ventilator

Volume Ventilator In a volume ventilator, constant volume of air is pumped into the lungs intermittently with minimum pressure.

Pressure Ventilator In a pressure ventilator, air is pumped into the lungs of the subject with constant high pressure.

Complications Mechanical ventilation has direct and indirect effects on the lung and upper airways, the cardiovascular system, and the gastrointestinal system. Pulmonary complications include barotraumas, nosocomial pneumonia, oxygen toxicity, tracheal stenosis, and deconditioning of respiratory muscles.

8.3.3 Hypoxia

Hypoxia means deprivation of oxygen. It is a pathological condition. If the body as a whole is deprived of oxygen supply, it is called **generalized hypoxia**. Suffocation, cardiac arrest, head trauma, carbon-monoxide poisoning and complications of general anesthesia can create conditions that can lead to cerebral hypoxia. Symptoms of mild cerebral hypoxia include inattentiveness, poor judgment, memory loss, and a decrease in motor coordination. Brain cells are extremely sensitive to oxygen deprivation and can begin to die within three minutes

after oxygen supply has been cut off. When hypoxia lasts for a longer period, it can cause coma, seizures, and even brain death.

In shock, hypoxia results in cell damage and there is release of chemical substances. Permeability of capillaries increases. Fluid comes out into the tissues which cause hypovolemia and further shock and the cycle goes on.

When the oxygen-carrying capacity of blood is reduced, e.g., in hemorrhage or at high altitudes where the oxygen tension in the air is reduced, hypoxia results, which stimulates erythropoietin formation and thus increases erythrocyte formation (erythropoiesis).

The order of symptoms in general varies among individuals: increased breathing rate, headache, light-headedness, dizziness, tingling or warm sensations, sweating, poor coordination, impaired judgment and euphoria. When a region of the body is deprived of oxygen supply, it is called **tissue hypoxia**.

When there is complete deprivation of oxygen supply it is called **anoxia**.

There are four types of hypoxia:

- The **hypoxemic type**, in which the oxygen pressure in the blood going to the tissues is too low to saturate the hemoglobin.
- The **anemic type**, in which the amount of hemoglobin is low, and hence the capacity of the blood to carry oxygen is low.
- The **stagnant type**, in which the blood is normal but the flow of blood to the tissues is reduced.
- The **histotoxic type**, in which the tissue cells are poisoned and are, therefore, unable to use oxygen.

Diseases of the blood, the heart and circulation, and the lungs may all produce some form of hypoxia.

Cerebral hypoxia is a condition in which there is a decrease of oxygen supply to the brain, even though there is adequate blood flow. Unless detected early and dealt with, hypoxia can be dangerous.

8.4 ABNORMAL TYPES OF BREATHING

1. Dyspnea

Dyspnea means shortness of breath. There is difficulty in breathing or labored breathing. The person struggles to breathe.

Pathophysiology It could occur due to lung diseases like asthma, bronchitis, pneumonia, lung cancer, emphysema and chronic obstructive lung disease. Pleural effusion can cause marked dyspnea.

Cardiac conditions can result in dyspnea. Children with congenital heart defects can develop dyspnea due to lack of oxygen.

Persons with abnormality of the spine or rib cage or with injury to these structures can cause dyspnea.

Dyspnea is seen in panic attacks also.

2. Cheynes–Stokes Breathing

Cheynes–Stokes breathing is an abnormal type of breathing characterized by increase in depth and rate of respiration followed by a decrease, resulting in apnea. It is usually seen in comatose persons having diseased nervous centers of respiration.

It is seen in coma, severe chronic heart failure, stroke, head injury, uremia, raised intracranial pressure and opium poisoning. It signifies impending death.

It is also seen in children during sleep and at high altitudes (physiological).

Pathophysiology Due to accumulation of CO_2, there is increase in the rate and depth of respiration. This is hyperpnea. With fast and deep breathing, CO_2 is washed out. Hence, the level of CO_2 in the lungs decreases. There is stoppage of breathing—this is apnea. This leads to CO_2 accumulation and breathing again starts, and the cycle goes on.

3. Apnea

Apnea means absence of breathing. It normally occurs in the sleep patterns of people who snore. Apnea is seen in sudden rise in blood pressure and after vagal stimulation. Apnea is a dangerous condition and if it lasts for more than few minutes it could end in death. Hence, it has to be monitored closely.

4. Cyanosis

Cyanosis is a blue discoloration of the skin and mucous membrane. It can be local or general. It is usually seen first on the lips, nails, tip of the nose and the ear lobules.

Pathophysiology It occurs when the deoxygenated hemoglobin in blood vessels near the surface is more than, or equal to, 2.5 g/dL. Low blood oxygen may be caused by poor blood circulation, or heart or breathing problems. It can also be caused by being in a low-oxygen environment or by carbon-monoxide poisoning or poisoning from chemicals or drugs.

It is seen in infants at birth due to congenital heart disease, in which some of the blood is not pumped to the lungs for oxygenation.

5. Asphyxia

Asphyxia is a condition in which there is decrease in the amount of oxygen in the blood accompanied by an increase of

carbon dioxide, causing inability to breathe and suffocation. If it is prolonged, it could lead to fall in blood pressure, loss of consciousness, cyanosis and death.

Pathophysiology Lack of oxygen can occur due to choking, gas leak, carbon-monoxide poisoning, drowning, strangulation, diphtheria, asthma, foreign body in the trachea, pneumothorax, and heart failure.

Fetal asphyxia is asphyxia in-utero due to hypoxia.

Traumatic asphyxia is due to sudden and severe compression of the thorax or upper abdomen.

Other forms of abnormal breathing are shallow breathing and Kussmaul respiration.

Kussmaul respiration causes hyperventilation, prolonged inhalation and persistent hyperventilation which may be caused by a central-nervous-system disorder.

Shallow breathing is respiration that fills the lungs only partially.

8.5 RESPIRATORY DISORDERS

1. Pharyngitis

Pharyngitis is an inflammation of the throat or pharynx. It is painful and lasts for a lengthy period. It could be acute or chronic. It could be associated with enlarged tonsils or with upper-respiratory-tract infection.

Pathophysiology Most of the cases (40 to 80%), are caused by viral infections. The rest are caused by bacterial infections, fungal infections or by irritants like pollutants, smoke or chemical substances.

Most of the time it follows due to an infectious organism acquired from close contact with an infected person.

It is also seen in diphtheria, gonorrhea, acute HIV infection and common cold associated with postnasal drip.

2. Laryngitis

Laryngitis is an inflammation of the larynx or voice box. It could be acute or chronic. Here, the voice becomes hoarse.

Pathophysiology The most common cause of laryngitis is common cold or flu, usually caused by a virus.

Another cause of laryngitis is overuse of the voice like shouting or talking for a long time.

It can occur due to exposure to an irritant like smoke or dust.

Acid reflux is the most common cause of chronic laryngitis and is also called **reflux laryngitis**.

Chronic laryngitis is also seen in bacterial infections like tuberculosis or nerve damage or nodules on the vocal cords.

3. Bronchitis

Bronchitis is an inflammation of the mucous membrane of the bronchi. There are several types of bronchitis but the two most common are acute and chronic types.

Pathophysiology Acute bronchitis is usually caused by infectious agents like bacteria or viruses. It may, also, be caused by physical agents or chemical agents like dusts, allergens, strong fumes or tobacco smoke. It may happen as a result of an asthma attack.

It may, also, follow common cold or upper-respiratory-tract infection.

Chronic bronchitis is a chronic infection of the bronchi associated with persistent cough resulting in sputum production for more than three months every year for more than 3 years.

4. Tuberculosis

Tuberculosis is a chronic bacterial infection of the lungs. Other organs are also sometimes involved.

Pathophysiology Tuberculosis is an air-borne disease. Yet, repeated exposure to the germs is usually necessary before a person gets infected. It is caused by the bacteria *Mycobacterium tuberculosis*.

It affects all ages, races and males and females equally.

Those who are at higher risk are the following–people living in poor environmental conditions, people who live or work with those who have tuberculosis, those who abuse alcohol, those who use repeated intravenous drugs, health workers who come in contact with high-risk populations and people with impaired immune systems.

5. Chronic Obstructive Lung Disease

Chronic obstructive lung disease is a physiologic abnormality. It is caused by major disorders like asthma, chronic bronchitis, emphysema and bronchiectasis. There is obstruction to the passage of air through the airways. It is characterized by decreased airflow rates during expiration, associated, often, by an elevated functional residual capacity due to trapped air.

6. Asthma

Asthma is a chronic inflammatory disorder of the airways characterized by episodic airway narrowing and increased reaction of the airway to various stimuli. There is spasmodic contraction of the bronchi and bronchioles. Mucous membrane is congested and inflamed. Excessive secretion of mucous is present. This leads to difficulty in breathing as there is resistance to the passage of air. Expiration is more labored than inspiration.

7. Emphysema

It is an abnormal enlargement of the air spaces due to progressive destruction of alveolar walls. Sometimes, these abnormal air spaces coalesce to form giant, essentially nonfunctional, air spaces called **bullae** which compress surrounding areas of the normal lung. The degree of obstruction correlates most closely with the severity of the emphysema. Vital capacity is decreased.

8. Bronchiectasis

It is a disease of the lung where there is abnormal and persistent dilatation of the bronchi, especially the smaller bronchioles, resulting from destructive changes in the elastic and muscular layers of the bronchial walls. It could be localized or diffuse. Spaces are formed which get infected and filled with purulent material which comes out as sputum.

9. Pneumonia

It is an inflammation of the lungs caused by bacteria, viruses, or chemical irritants. It could become serious when the air sacs fill with pus and infectious liquid. Lobar pneumonia affects one or more sections of the lungs. Bronchial pneumonia affects patches throughout the lungs.

Pathophysiology Bacterial pneumonia is caused by various bacteria of which *Streptococcus pneumoniae* is the most common bacterium.

Pneumonia occurs in those whose body becomes weak due to chronic illness, old age, malnutrition, or decreased immunity.

High risk factors are those who consume alcohol, debilitated persons, weak immune systems, other respiratory infections and contact with the infected person.

Viral pneumonia is caused by various viruses.

Mycoplasma pneumonia is caused by mycoplasmas.

10. Lung Abscess

Lung abscess is defined as pulmonary parenchymal necrosis due to infection and results in cavity formation.

Pathophysiology It is due to severe microorganism invasion of lung tissue. There is also inadequate clearance of the airways. It also follows aspiration of foreign material.

11. Pleural Effusion

The pleural space contains a small amount of serous fluid. When there is an excess quantity of fluid in this pleural space, it is called pleural effusion.

Pathophysiology Fluid enters the pleural space from the capillaries in the parietal pleura and is removed via the lymphatics situated in the parietal pleura. Pleural fluid accumulates when pleural-fluid formation exceeds pleural-fluid absorption.

It occurs as a result of lung diseases like tuberculosis, carcinoma or pneumonia.

12. Pneumothorax

Pneumothorax is the presence of gas in the pleural space.

Pathophysiology Spontaneous pneumothorax occurs without any history of trauma to the thorax. Primary spontaneous pneumothorax occurs without underlying lung disease. Secondary spontaneous pneumothorax occurs secondary to lung disease. Traumatic pneumothorax occurs from a penetrating or nonpenetrating injury to the thorax.

13. Carcinoma of the Lung

Carcinoma of the lung is a disease of uncontrolled cell growth in the tissues of the lung. This growth can lead to metastasis. There is chest discomfort, weight loss, cough and hemoptysis.

Pathophysiology Smoking tobacco is the main cause of lung cancer.

It occurs due to carcinogens in the form of tobacco smoke, ionizing radiation and viral infection. The exposure causes cumulative changes to the DNA in the tissue lining the bronchi of the lungs. As more and more tissue gets damaged, it terminates in cancer.

Genetic mutations in the epidermal growth-factor gene are probably responsible.

Other risk factors are arsenic, asbestos, mustard gas, coke-oven emissions or nickel, are all carcinogens. They could be breathed or people may work in factories and be exposed to these carcinogens.

REVIEW QUESTIONS

1. Explain the general anatomy and physiology of the respiratory system with a diagram.
2. Describe the anatomy of nasal cavity with applied anatomy and functions.
3. Describe the anatomy of pharynx with applied anatomy and functions.
4. Describe the anatomy of larynx with applied anatomy and functions.
5. Describe the action of respiratory muscles.
6. Describe the anatomy of pleura with applied anatomy and functions.
7. Discuss the general features of lungs. Give the differences between right and left lungs.
8. Describe the mechanism of respiration.
9. How is respiration regulated?
10. Describe various pulmonary volumes and capacities. Discuss in brief the significance of timed vital capacity.
11. Explain exchange of gases between lung and tissues.
12. Describe the various abnormal types of breathing.
13. Briefly discuss the various respiratory disorders with their pathophysiology.
14. Discuss pulmonary function tests.
15. Write short notes on:
    a. Artificial respiration
    b. Bronchopulmonary segments
    c. Trachea
    d. Mediastinum
    e. Respiratory bronchioles and alveoli
    f. Hypoxia

Chapter

9 Digestive System

- **DIGESTIVE SYSTEM**
  - Structure ..... Mucosa, Submucosa, Muscular, Serous
  - Peritoneum ..... Applied anatomy ..... Arterial supply
    ..... Venous drainage
    ..... Nerve supply
- **MOUTH**
- **TONGUE**
  ..... Arterial supply
  ..... Venous drainage
  ..... Nerve supply
- **TEETH**
  ..... Functions ..... Arterial supply
  ..... Venous drainage
  ..... Nerve supply
- **SALIVARY GLANDS**
  ..... Parotid, Submandibular, Sublingual ..... Arterial supply
  ..... Venous drainage
  ..... Nerve supply
  ..... Saliva
  ..... Functions
- **ESOPHAGUS**
  - Structure ..... Arterial supply
    ..... Venous drainage
    ..... Nerve supply
  - Functions
- **STOMACH**
  - Structure ..... Arterial supply
    ..... Venous drainage
    ..... Nerve supply

- Functions
- Gastric juice ..... Functions

- **SMALL INTESTINE**
  - ..... Duodenum
  - ..... Jejunum
  - ..... Ileum
- Structure ..... Arterial supply
  - ..... Venous drainage
  - ..... Nerve supply
- Movements ..... Mixing, Propulsive, Peristaltic
- Functions

- **LARGE INTESTINE**
  - ..... Caecum, Ascending colon, Transverse colon, descending colon, sigmoid colon, rectum, anal canal,
- Structure ..... Serous, muscular, submucosal
  - ..... Arterial supply
  - ..... Venous drainage
- Movements
- Functions

- **PROCESSES IN DIGESTION**
  - ..... Mastication
  - ..... Swallowing
  - ..... Digestion
  - ..... Absorption
  - ..... Defaecation ..... Faeces

- **PANCREAS**
  - ..... Arterial supply
  - ..... Venous drainage

- **LIVER**
- Relations
- Lobes
- Functions ..... Carbohydrate metabolism
  - ..... Protein metabolism
  - ..... Fat metabolism

- **BILIARY TRACT**

- **GALL BLADDER**

  - Arterial supply
  - Venous drainage
  - Nerve supply

  - Functions

  - Bile ..... Functions

- **DISORDERS**

  - Nausea
  - Anorexia
  - Vomiting
  - Diarrhea
  - Constipation
  - Dysphagia
  - Flatulence
  - Heartburn
  - Gastritis
  - Gastroenteritis
  - Peptic ulcer
  - Cholecystitis
  - Appendicitis
  - Peritonitis
  - Hepatitis
  - Fatty liver
  - Cirrhosis of liver
  - Jaundice

Introduction

Digestion is the process by which food is broken down into smaller and simpler substances, to be used for the purpose of nourishment of the cell, in order to provide energy to the body. Digestion involves mixing of food, downward movement through the digestive tract and the breakdown of larger molecules into smaller molecules, which can be absorbed easily.

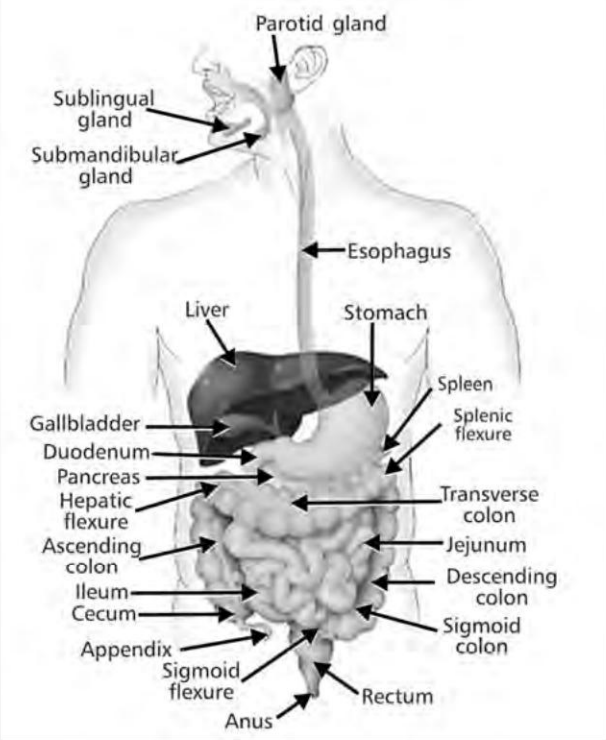


Fig. 9.1 *Organs of alimentary system*

9.1 DIGESTIVE SYSTEM

The digestive system starts from the mouth and ends at the anus. It includes the esophagus, stomach, small intestine and large intestine, together with the liver, gall bladder and pancreas, which produce important secretions—enzymes—for digestion. They all drain their juices into the small intestine.

9.1.1 Structure

The basic structure of the digestive system starts from the esophagus.

The wall of the digestive tract has four layers:

1. Mucosa
2. Submucosa
3. Muscular layer
4. Serous layer or serosa

1. Mucosa

It is the innermost layer of the wall which lines the lumen of the digestive tract. It consists of a layer of columnar epithelium. Next is a layer of loose connective tissue called **lamina propria** which has blood vessels and lymphatics. There is an outer thin layer of smooth muscle called the **muscularis mucosa**. In certain regions, the mucosa develops folds which increase the surface area for absorption. Certain cells in the mucosa secrete mucus, digestive enzymes and hormones. Mucosa protects and carries out the function of absorption. In the mouth and anus, the epithelium is stratified squamous type, where thickness for protection against abrasion is needed. The stomach and intestines have a thin simple columnar epithelial layer for secretion and absorption.

2. Submucosa

It is a thick layer of loose connective tissue with few elastic fibers. It surrounds the mucosa. This layer contains blood vessels, lymphatic vessels and nerves. Glands may be seen embedded in this layer. The blood vessels are the arterioles, venules and capillaries. The nerve plexus is called the **Meissner's plexus**. It has both sympathetic and parasympathetic fibers.

3. Muscular Layer

It is arranged in two layers, an inner circular layer and an outer longitudinal layer. The mesenteric plexus lies between these two muscle layers. There are, also, blood vessels and lymph vessels. This layer is responsible for peristaltic movements which push the food downwards. It also helps the food to mix with the digestive juices. At some places, they form sphincters or valves.

4. Serous Layer or Adventitia

Above the diaphragm, in the thorax, this layer consists of connective tissue called adventitia. Below the diaphragm, the organs have a serous covering called serosa or peritoneum.

9.1.2 Peritoneum

The peritoneum is the serous membrane that forms the lining of the abdominal cavity or the coelom. It covers and supports most of the intra-abdominal organs and also serves as a medium for their blood vessels, lymph vessels and nerves.

It consists of two layers with a potential space between them.

The outer layer, called the **parietal peritoneum**, is attached to the abdominal wall.

The inner layer, called the **visceral peritoneum**, covers the internal organs that are located inside the intraperitoneal cavity.

The **potential space** between these two layers is the cavity which is filled with a small amount (about 50 mL) of serous fluid that allows the two layers to slide freely over each other. The space is actually outside the peritoneal sac, and thus, not in the peritoneal cavity.

The mesentery is the part of the peritoneum through which most abdominal organs are attached to the abdominal wall and are supplied with blood, lymph vessels and nerves.

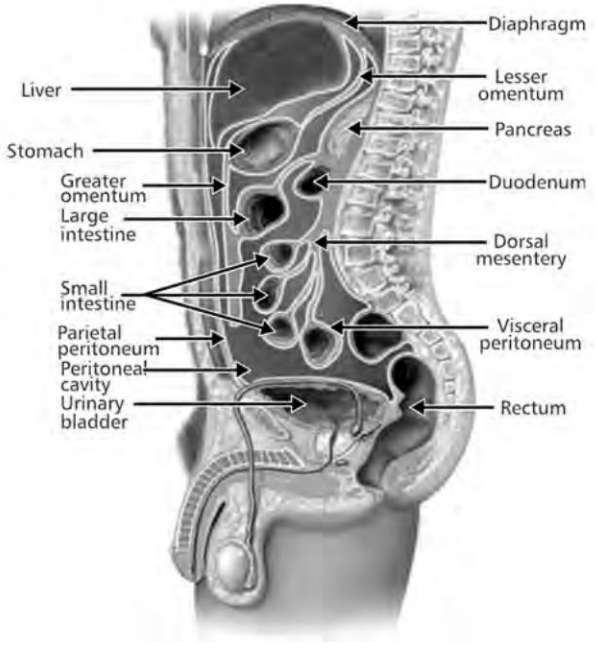


Fig. 9.2 *Peritoneum and peritoneal cavity*

The abdominal organs could be intraperitoneal, retroperitoneal or infraperitoneal, depending on whether they are covered with visceral peritoneum and have mesentery or not.

- **Intraperitoneal** organs are liver, spleen, uterus, stomach, small intestine, cecum, transverse colon, sigmoid colon and upper 1/3rd of the rectum.
- Kidneys, adrenals, proximal ureters, pancreas, middle1/3rd of rectum and aorta are **retroperitoneal.**
- Lower 1/3rd of rectum, urinary bladder and distal ureters are **infraperitoneal**.

Intraperitoneal structures are usually mobile while retroperitoneal organs are more or less fixed.

Applied Anatomy

1. **Peritonitis** is an inflammation of the peritoneal lining or cavity. It can occur due to infection of any abdominal organ or secondary to perforation of a viscus. In severe or advanced cases, surgery may be required.
2. Accumulation of fluid in the peritoneal cavity is called **ascites** and can occur in generalized conditions like anemia with hypoproteinemia, in conditions like cirrhosis of liver, tuberculosis or malignancy or as a part of **anasarca** (generalized edema).
3. Pneumoperitoneum is the presence of gas within the peritoneal cavity and can occur due to perforation of the stomach or intestines. This is a serious condition.
4. Peritoneal dialysis is carried out in renal failure to remove waste products.

(a) Arterial Blood Supply Branches from thoracic aorta supply the esophagus; celiac artery supplies the stomach, liver, pancreas and biliary apparatus while duodenum and mesenteric arteries supply the small intestine and large intestine. The distal part of the rectum and anus are supplied by rectal arteries.

(b) Venous Drainage Veins from the upper esophagus drain into esophageal veins; veins from lower esophagus, stomach, small and large intestine into the portal vein. Veins from the lower rectum and anus drain into internal iliac veins.

(c) Nerve Supply Most of the parasympathetic supply is through the vagus nerve. Sacral nerves supply the most distal part of the large intestine.

The sympathetic supply is derived from plexuses in the thorax, abdomen and pelvis.

9.2 MOUTH

The mouth or **buccal cavity**, or **oral cavity** is the first portion of the alimentary canal. It is bounded anteriorly by the lips. Laterally lie the alveolar arches with the teeth, superiorly are the hard and soft palate and posteriorly it is continuous with the pharynx. It is moist, and lined with a mucous membrane which is stratified squamous epithelium and contains mucous-secreting glands. It is continuous with the skin through the lips. It receives food. Digestion begins here by mechanically breaking the solid food particles into smaller pieces and mixing them with saliva.

Through the open mouth the **uvula** can be seen, hanging from the soft palate. From the uvula four folds of mucous membrane pass laterally forming arches and between them lies the **palatine tonsil**.

Besides digestion, the mouth plays an important role in speech, breathing and facial expressions.

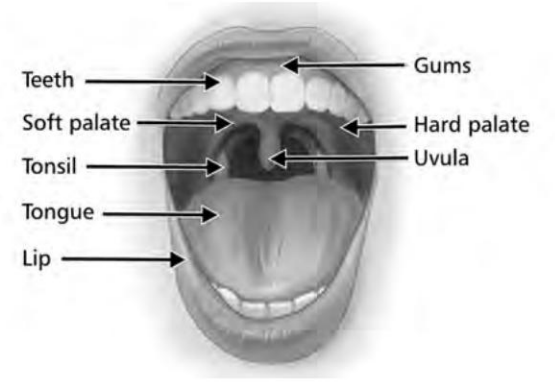


Fig. 9.3 *Oral cavity*

9.3 TONGUE

The tongue is a voluntary muscle on the floor of the mouth, which is necessary for chewing and swallowing (deglutition). It is the primary organ of taste, which is attached (by its base to the hyoid bone and to the floor of the mouth) by a fold of mucous membrane called the **frenulum**. It extends past the posterior border of the mouth and into the oropharynx.

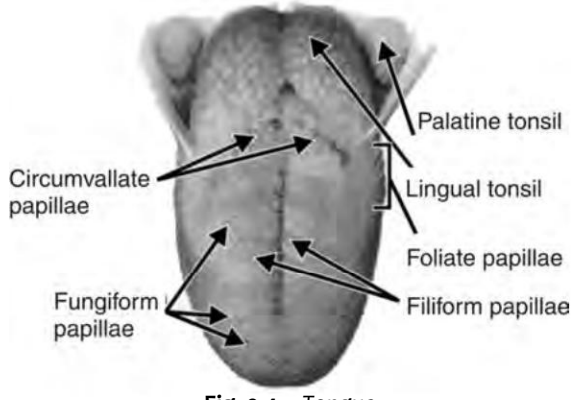


Fig. 9.4 *Tongue*

It is divided into two parts—an oral part (anterior two-thirds of the tongue) that lies mostly in the mouth and a pharyngeal part (posterior third of the tongue), which faces backward to the oropharynx. These two parts are separated by a V-shaped groove.

It is covered by stratified squamous epithelium. There are papillae on its surface (details in the chapter of physiology of taste).

(a) Arterial Supply The main arterial supply is by the lingual branch of the external carotid artery.

(b) Venous Drainage Venous drainage is into the lingual vein which drains into the internal jugular vein.

(c) Nerve Supply Nerve supply is by the hypoglossal nerve which supplies the muscles of the tongue; the facial and glossopharyngeal nerves are for taste sensation, and lingual branch of mandibular nerve is for sensations.

It carries out the important functions of mastication, deglutition, taste and speech.

9.4 TEETH

There are 32 teeth embedded in the alveoli of the alveolar ridge of the mandible and the maxilla. The teeth are arranged from front to back—incisors, canine, premolars and molars.

Each tooth has three components—crown, neck and root. The **crown** protrudes from the gum. The neck is embedded in the bone and the **root** is the narrow part where the crown merges with the root.

The tooth is made up of dentine, enamel and cementum. **Dentine** has an ivorylike structure and forms the major part of the tooth. **Enamel** is harder than bone and is the outermost covering that covers the crown of the tooth. **Cementum** is as hard as bone and is in the neck of the tooth. In the center of the tooth is the **pulp cavity** which contains blood vessels, lymph vessels and nerves. It is surrounded by the dentine.

Functions of the Teeth

- The front teeth, canine and incisors, are for biting and cutting.
- The back teeth, premolars and molars, are for crushing, chewing and grinding.

(a) Arterial Supply The arterial supply is by the branches of the maxillary arteries.

(b) Venous Drainage The venous drainage is by many veins which drain into the internal jugular veins.

(c) Nerve Supply Nerve supply is by the branches of the trigeminal nerve—upper teeth are supplied by the branches of the maxillary nerve, and lower teeth by the branches of the mandibular nerve.

9.5 SALIVARY GLANDS

Saliva is produced and secreted from salivary glands. There are three major pairs of salivary glands in the mouth. The largest pair is called the **parotid gland**. Two smaller pairs, the sublingual glands and the submandibular glands, lie in the floor of the mouth. There are many tiny salivary glands distributed throughout the mouth.

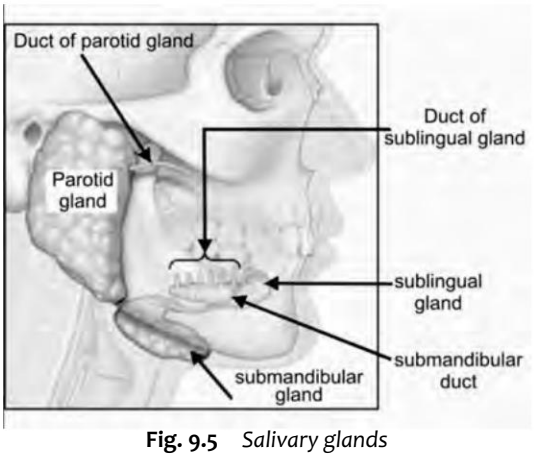


Fig. 9.5 *Salivary glands*

The **parotid** glands, one on each side, lie just behind the angle of the jaw, below and in front of the ears. The parotid duct opens into the mouth at the level of the upper second molar tooth.

The **submandibular** glands lie near the inner side of the lower jawbone. They are rounded in shape. Ducts open on the floor of the mouth on either side of the frenulum.

The **sublingual** glands lie directly under the mucous membrane covering the floor of the mouth beneath the tongue. Many small ducts open directly into the floor of the mouth.

The basic secretory units of salivary glands are clusters of cells called **acini**.

There are two basic types of acinar epithelial cells—**serous cells**, which secrete a watery fluid, essentially devoid of mucus; and **mucus cells**, which produce mucus-rich secretion.

The fluid which contains water, electrolytes, mucus and enzymes enters the collecting duct. Small collecting ducts within salivary glands lead into larger ducts, eventually forming a single large duct that empties into the oral cavity.

Within the ducts, the sodium is actively reabsorbed, potassium is secreted, and large quantities of bicarbonate ions are secreted.

(a) Arterial Supply By branches from the external carotid arteries.

(b) Venous Drainage Into the external jugular veins.

(c) Nerve Supply By parasympathetic (increases secretion) and sympathetic (decreases secretion) fibers.

9.5.1 Saliva

About 1.5 liters of saliva is produced and secreted per day, by three pairs of salivary glands.

Saliva contains 99.5% of water, but also includes electrolytes, mucus, immunoglobulins, blood-clotting factors and various enzymes like salivary amylase, pepsin, lipase and lysozymes.

Saliva secretion occurs as soon as food enters the mouth; the sight or smell or even the thought of food can stimulate saliva secretion.

Parasympathetic stimulation causes vasodilatation and release of watery saliva with low enzyme and organic content. Sympathetic stimulation causes vasoconstriction and releases small amount of saliva rich in organic substances.

Functions

1. Food is moistened and lubricated and made soft into a bolus.
2. It lubricates and protects the teeth and the tongue. It dilutes hot and pungent substances and thus prevents damage to the tender tissues inside the mouth and the mucous membrane.
3. It keeps the mouth moist and facilitates speech.
4. The enzymes in the saliva break down some of the starch and fat in the food at the molecular level. Starch is split into maltose and maltase changes maltose into glucose which gives a sweet taste to the food. Fats are emulsified to fatty acids and glycerol. Pepsin converts proteins to peptones.
5. It also breaks down food caught in the teeth, protecting them from bacteria that cause decay of teeth.
6. It also plays an important role in tasting food. Saliva mixes with the food and the taste buds are stimulated by the chemical substances which are in solution.
7. Saliva helps in maintenance of water balance. Hence, if saliva secretion decreases, the tongue becomes dry and the person feels thirsty.
8. Saliva acts as a buffer by maintaining the level of bicarbonate and phosphate in the blood.
9. Microbes are attacked by lysozymes, clotting factors and immunoglobulins.

Note: *Pharynx* is discussed with the respiratory system.

9.6 ESOPHAGUS

The esophagus is a muscular tube that extends from the pharynx, down through the neck and the thorax, and through the diaphragm to the stomach. It is about 22 to 25 cm long and 2 cm in diameter. It is divided into cervical, thoracic, and abdominal parts.

In the neck it lies behind the lower end of the larynx and the upper part of the trachea. In the thorax, it continues behind the trachea and the heart. It passes down and opens into the stomach by passing through an opening between the muscle fibers of the diaphragm. The esophagus curves upwards before joining the stomach and this curve probably prevents regurgitation of the food which has entered the stomach. Muscles encircling

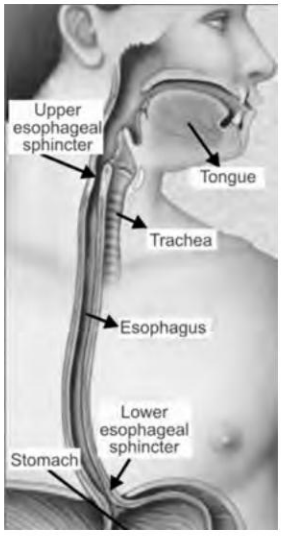


Fig. 9.6 *Esophagus*

the esophagus at the top form the **cricopharyngeal sphincter** which prevents sucking of air during inhalation and aspiration of esophageal contents during deglutition. The sphincter at the lower end is called the **cardiac sphincter** which prevents regurgitation of stomach contents.

9.6.1 Structure

It consists of three layers. The outer covering is made up of loose connective tissue called the **tunica adventitia**. The muscular layer is striated in the upper one third, unstriated or smooth muscles in the lower third, and mixed type in the middle. It is supplied with autonomic nerve fibers. There is a layer of submucosa consisting of elastic and collagenous connective tissue which contains nerve plexuses and blood vessels. The inner lining consists of folded mucous membrane. It is of striated type in upper third, columnar type in distal third and mixed variety in the middle.

(a) Arterial Supply Thoracic region is supplied by esophageal arteries which are the branches of the aorta. The abdominal region is supplied by inferior phrenic artery branches and coeliac artery.

(b) Venous Drainage It is from thoracic region into azygos and hemiazygos veins, and from abdominal region into left gastric vein.

(c) Nerve Supply Sympathetic and parasympathetic supply end in mesenteric and submucosal plexuses.

9.6.2 Functions

The function of the esophagus is to let the food pass from pharynx to the stomach by the process of deglutition—food enters the esophagus and is then propelled onwards by waves of contraction in the segment above and muscle relaxation below it. Mucus lubricates the wall and helps the food pass down. Peristaltic waves occur only when food enters the esophagus, otherwise it is relaxed. When food comes at the lower end, the pyloric sphincter opens and food enters the stomach. The pyloric sphincter remains constricted and prevents gastric acid reflux. The sharp angle between the stomach and esophagus also prevents reflux. Pinching effect of diaphragm and its attachment to stomach through the peritoneum also help in preventing gastric reflux.

9.7 STOMACH

The stomach is the most dilated part of the alimentary tract and is J-shaped. It lies between the end of the esophagus and the beginning of the small intestine. It occupies the epigastric, umbilical, and left hypochondriac regions of the abdominal cavity. It lies in a recess bounded anteriorly by the left lobe of the liver and anterior abdominal wall and the diaphragm, and posteriorly by spleen, pancreas, adrenal gland and abdominal aorta.

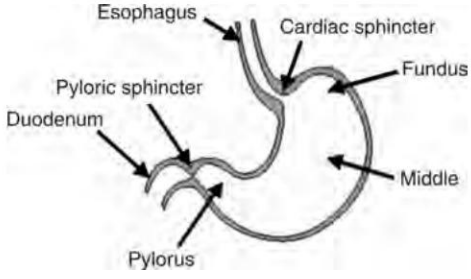


Fig. 9.7 *(a) Stomach*

It has two curvatures. The lesser curvature is short, extending between the cardiac and pyloric orifices and forms the right border of the stomach. It descends as a continuation of the right margin of the esophagus. The greater curvature is four or five times as long as the lesser curvature. It starts from the cardiac orifice, forms an arch with a slight convexity to the left, turns to the right to end at the pylorus.

9.7.1 Structure

The stomach is divided into four parts—cardia, fundus, body and the antrum. The **cardia** is closest to the heart and the esophagus is connected to the stomach at this end. The **fundus** lies above the level of the cardiac sphincter and is the upper part of the stomach. The **body** is the largest region located in the center. The **pylorus** is divided into pyloric antrum and a

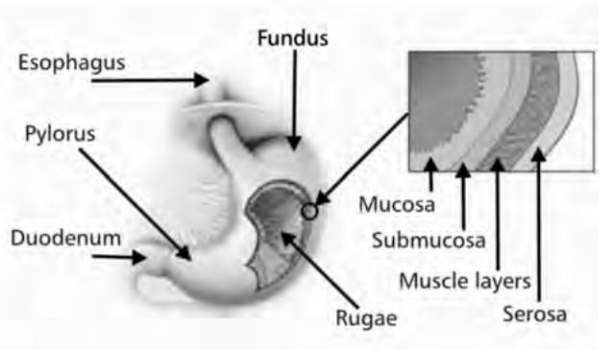


Fig. 9.7 *(b) Stomach*

canal after the antrum and is connected to the small intestine. The cardia and the pylorus have sphincter muscles—cardiac sphincter and pyloric sphincter.

The wall consists of four layers—the serosa, the muscularis, the submucosa, and the mucosa. **Serosa** is made of areolar connective tissue. The muscle layer consists of an outer longitudinal layer, a middle circular layer, and an inner oblique layer. Submucosa consists of loose connective tissue which contains blood vessels and nerve plexuses. The mucosa is thicker and consists of numerous folds called **rugae**. There are numerous tubular glands (30 million glands) in the mucosa which contain cells that secretes gastric juice.

Secretory glands are of three types:

- Peptic glands which secrete pepsin,
- Oxyntic glands which secrete hydrochloric acid, and
- Mucus glands that secrete mucus.

The fundus chiefly contains oxyntic glands, the body has peptic glands and mucus glands are found in the pyloric portion.

(a) Arterial Supply It is by branches of coeliac artery.

(b) Venous Drainage It is into the portal vein.

(c) Nerve Supply Sympathetic supply is from the coeliac plexus. Its stimulation decreases gastric secretion and motility. Parasympathetic supply is via the vagus nerve, stimulation of which increases motility and secretion.

9.7.2 Functions

1. The primary function of the stomach is to act as a temporary storage area for food and to initiate the digestive process.
2. The stomach helps with the mechanical break-up of food. Waves of contraction churn the food and break the food into smaller particles, so that it is easier to digest, and helps to mix it with gastric juices.
3. It holds food temporarily and releases it steadily at a constant rate into the duodenum. The pyloric sphincter is closed when the stomach is active. Once the food is digested and liquefied, a small amount is pushed into the duodenum with the opening of the sphincter.
4. It secretes a hormone called **gastrin** which stimulates acid secretion by the stomach.
5. It produces an intrinsic factor which is necessary for absorption of vitamin B12, important for the formation and maturation of red blood cells.
6. It secretes gastric juice which converts food into chyme thus facilitating digestion.
7. Mucus which is secreted, forms a lining for the stomach and so protects the wall of the stomach from the effect of gastric juices, hydrochloric acid and digestive enzymes.
8. Hydrochloric acid provides defense against microbes. It kills ingested parasites and harmful bacteria.
9. It helps in the excretion of some toxins and drugs.
10. Pancreatic and biliary secretions are stimulated when food enters the stomach.
11. It has a reflex function—**gastro-salivary reflex**, leading to secretion of salivary juice; **gastro-iliac reflex**, leading to peristalsis in the lower part of the ileum when food enters the stomach; and **gastro-colic reflex** producing mass peristalsis and stimulating defecation.

9.7.3 Gastric Juice

Gastric juice is a strong acidic liquid, with a pH varying from 1 to 3. It is almost colorless, and is secreted by the glands in the lining of the stomach.

There are several mechanisms responsible for the secretion of gastric juice. The stomach begins its production of gastric juice while the food is in the mouth. Nerves from the cheek and tongue are stimulated and send messages to the brain which in turn send messages to the nerves in the stomach wall. This stimulates the secretion of gastric juice even before the food arrives. When food arrives in the stomach and comes in contact with the mucosa, it stimulates some more gastric-juice. This is the second mechanism of gastric-juice secretion.

When food comes in the stomach, extra gastric juice is not required for carbohydrates, but, when there is protein in the food, it requires a greater supply of gastric juice. Protein is broken into polypeptides and peptides, and these smaller molecules stimulate the stomach cells to release the hormone **gastrin** which circulates in the blood; and when it comes to the stomach, it stimulates the stomach cells to secrete more gastric juice. The more protein there is in the stomach, more gastrin is produced and greater the production of gastric juice. This increased secretion in response to increased protein represents the third mechanism of gastric-juice secretion. There are thus three phases involved in gastric-juice secretion:

Cephalic phase, gastric phase, intestinal phase.

(a) Cephalic Phase Sight, smell or even the thought of food results in gastric secretion. This occurs due to reflex stimulation of vagus nerve.

(b) Gastric Phase Gastric secretion is stimulated by a number of hormones and chemical substances. The hormone gastrin is released into the bloodstream when peptides are detected in the stomach, and this stimulates the gastric glands to secrete more gastric juice. The main components are digestive enzymes (pepsin and acid), renin, mucus, water, mineral salts and intrinsic factor. This phase is the longest of all phases.

(c) Intestinal Phase When the partially digested food enters the small intestine, **enterogastrone**, an intestinal hormone, is released which reduces secretion of gastric juice and gastric motility. Gastric emptying is slowed down and duodenal contents now mix with pancreatic juice and bile.

Gastric emptying depends to a large extent on the type of meal taken. A carbohydrate meal empties in 2 to 3 hours. A meal with high protein content takes longer and a fat meal takes even more time.

Functions of Gastric Juice

1. Pepsin converts proteins into simpler substances that are absorbed and is helped by hydrochloric acid.
2. Renin aids the digestion of milk proteins, and milk caseinogen is converted into casein, which is digested by pepsin.
3. Mucus secreted by the gastric glands helps protect the stomach lining from the action of gastric juice and also protects the stomach from mechanical injury due to certain foods.
4. Certain cells of the stomach lining secrete a substance known as **intrinsic factor**. It is necessary for the absorption of vitamin B12 and its absence results in B12 deficiency which may ultimately lead to the development of pernicious anemia.
5. It helps liberate the fat of the food by dissolving the fibrous covering round its globules, preparing it for digestion in the duodenum.
6. Hydrochloric acid hydrolysis the food stuff. It also kills the microbes and stops the action of salivary amylase by creating an acidic medium.

9.8 SMALL INTESTINE

The small intestine is the largest and the longest part of the gastrointestinal tract. It is a convoluted tube, continuous from the pylorus to the colic valve, where it leads into the large intestine. It is about 6 to 7 meters (23 feet) long, and gradually

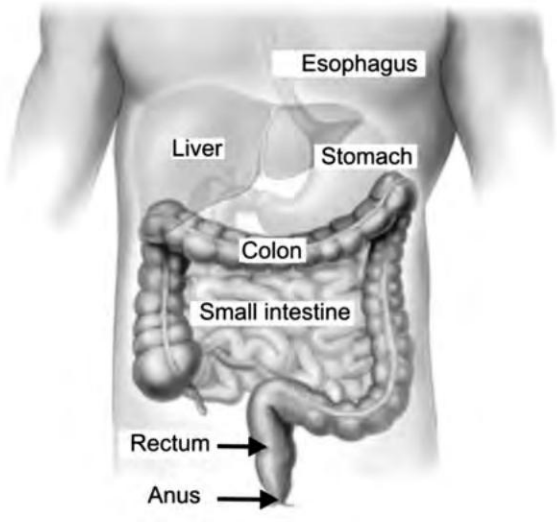


Fig. 9.8 *Intestines*

diminishes in size from its origin to its termination. It lies in the central and lower part of the abdominal cavity. It is surrounded, above and at the sides, by the large intestine Almost 90% of daily fluid intake is absorbed in the small intestine. Anteriorly, it is related to the greater omentum and is connected to the vertebral column by a fold of peritoneum, the mesentery.

It consists of three portions: the duodenum, the jejunum and the ileum.

1. Duodenum

The duodenum, starts from the stomach at the pyloric sphincter. It is about 25 cm long and is C-shaped. The head of the pancreas lies in the C-shaped duodenum. It is almost entirely retroperitoneal and is the most fixed part of the small intestine. It has four parts—superior part, descending part, horizontal part and ascending part. The fourth part joins the jejunum at the duodenojejunal flexure. The descending part contains openings of bile duct and pancreatic duct which open as the common bile duct. Here, it forms a common structure called

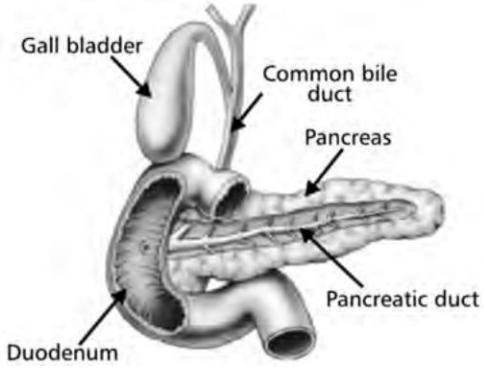


Fig. 9.9 *Duodenum*

the **hepatopancreatic ampulla**. It is guarded by a hepatopancreatic sphincter.

Food in the duodenum mixes with bile from the gall bladder and digestive enzymes from the pancreas. Absorption of vitamins, minerals and other nutrients begins in the duodenum.

2. *Jejunum*

The jejunum is the middle portion of the small intestine. It lies between the duodenum and the ileum. The change from the duodenum to the jejunum is usually defined as the **ligament of Treitz**. It is 2.5 meters long. It is suspended by the mesentery and hence it is mobile. The role of the jejunum is mainly digestion of food and absorption to some extent.

3. *Ileum*

The ileum is the lowest coiled portion of the small intestine beyond the jejunum, just before the large intestine. It is separated from the cecum by the ileocecal valve and joins it in the right lower quadrant near the appendix.

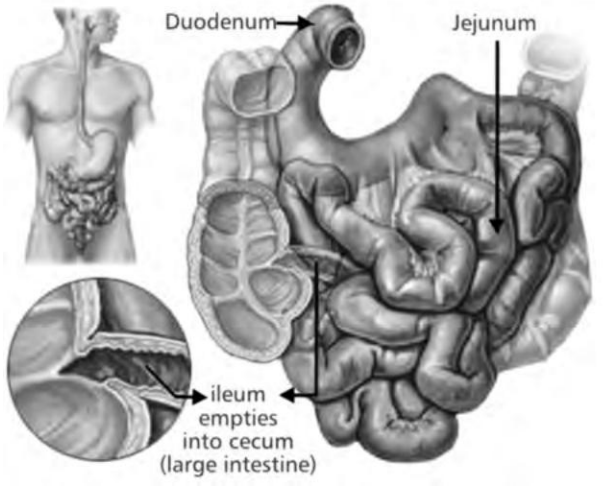


Fig. 9.10 *Ileum*

It is also suspended by the mesentery of the small intestines and, hence, is extremely mobile. The ileocecal valve controls flow of material from the ileum to the cecum and prevents regurgitation.

9.8.1 Structure of the Small Intestine

Exact boundaries between the three parts are not seen grossly or microscopically**. Serosa** is the outer layer. **Muscularis externa** consists of smooth muscles arranged in two layers—outer layer consisting of longitudinal fibers and inner layer consisting of circular fibers.

Submucosa consists of the **Brunner's glands**. The ducts of these glands open on the mucosa into the **Crypts of Lieberkiin**.

The inner surface of the small intestine—**mucosa**—is not flat, but thrown into circular folds. This increases surface area of tissue available to absorb nutrients from the gut contents and also helps in mixing the food. The mucosa forms projections called villi which protrude into the lumen and are covered with columnar epithelial cells called **enterocytes**. They increase the surface area of the intestinal wall. The membrane of these absorptive epithelial cells is studded with densely packed microvilli. These cells are surrounded by blood and lymph vessels. The lymph capillaries are called **lacteals**, which absorb digested food. Between the enterocytes are seen goblet cells which secrete mucus. Some digestion and most of the absorption takes place in the enterocytes.

Intestinal juice is secreted by the intestinal glands of the small intestine. It is about 1500 mL daily and its pH is 7.8 to 8.0. It contains water, mineral salts, mucus and the enzyme enterokinase.

Many lymph nodes are found in the mucosa throughout the length. They have defensive cells which help in defense mechanisms and neutralize antigens.

Digestive enzymes are produced and are secreted into the lumen, they lodge in the villi and mix with the intestinal juice, carry out the final digestion of proteins, carbohydrates and fats.

There are certain differences among the duodenum, jejunum and ileum.

The villi in the jejunum are much longer than in the duodenum or ileum.

The jejunum contains very few Brunner's glands which are found in the duodenum.

There are also few Peyer's patches in the jejunum which are found to be more in the ileum. The jejunum has many large circular folds in its submucosa called **plicae circulares** which increase the surface area for absorption.

Through the epithelial cells of the jejunum and ileum, there is passive transport of sugar fructose and the active transport of amino acids, small peptides, vitamins, and most glucose.

(a) Arterial Supply By superior mesenteric artery.

(b) Venous Drainage Into superior mesenteric vein which drains into the portal vein.

(c) Nerve Supply Sympathetic and parasympathetic innervation.

9.8.2 Movements of the Small Intestine

When food enters the small intestine, chemical digestion of the food gets completed and the process of absorption starts.

Different types of movement take place in the small intestine to facilitate propulsion of food and absorption. They are mixing movements, propulsive movements, peristaltic movements and movements of the villae.

Mixing movements are essential for mixing of the chyme with the digestive juices. These juices are the pancreatic juice, bile and intestinal juice. They are segmental and pendular movements. Segmental contractions occur in one segment of the intestine. The segment between the contracted segments is relaxed and length of both contracted and relaxed segments are the same giving a sausage (banana)like appearance to the intestine. Then the relaxed segment contracts and the contracted segment relaxes.

Propulsive movements move the chyme onwards. They are alternating contraction and relaxation waves. The contractions are in both the directions. The contractions which move towards the oral direction are inhibited while those which move towards the large intestine remain. Actually, these peristaltic waves start when the food is in the stomach, which is called gastroenteric reflex.

If there is excessive irritation of the mucous membrane of the small intestine, it causes powerful peristaltic contractions which push the contents fast. This is called **peristaltic rush**.

Sometimes, even when there is no food in the intestine, the stomach and intestine contract and propel the digestive secretions towards the colon.

The villi in the small intestine move simultaneously when the small intestinal movements are active. Presence of chyme initiates **movement of villi**. They shorten and elongate alternately. This facilitates absorption.

Peristaltic movements facilitate absorption. Absorption is also enhanced by the vast surface area made up of folds, villi, and microvilli.

9.8.3 Functions

The small intestine is that part of the digestive system where the most extensive process of **digestion** occurs.

It absorbs water and electrolytes, necessary for maintaining bodily systems and their functions. A sodium pump makes possible the absorption of water, nutrients and electrolytes. The small intestine contains different systems for extracting water and electrolytes, glucose, peptides, amino acids, and lipids. Through the mesentery it sends these elements from the intestine to the liver.

The function of all three sections of the intestine is to digest and absorb nutrients from food.

However, there are, also, specific functions of different parts of the small intestine.

The ileum passes food from the small intestine to the large intestine.

The jejunum performs the function of absorption to the maximum.

The lining of the small intestine secretes a hormone called **secretin**, which stimulates the pancreas to produce and release digestive enzymes.

The duodenum receives secretions from the liver, gall bladder and pancreas through bile ducts. It uses these secretions to extract nutrients from the food.

The chyme mixes with pancreatic juice, bile and intestinal juice.

Pancreatic juice contains many enzymes—amylase, lipase, trypsinogen, chymotrypsinogen and procarboxypeptidase. It is alkaline and on mixing with the acid in the stomach contents, the pH is increased, about 6 to 8. At this pH, amylase and lipase act.

Amylase converts polysaccharides to disaccharides. Maltose is converted to glucose.

Bile salts present in bile help in emulsification of fat and big molecules are reduced to smaller ones, increasing their surface area. They are then acted upon by lipase which converts them to fatty acids and glycerol.

Trypsinogen and chymotrypsinogen are activated by enterokinase and converted to trypsin and chymotrypsin which are now active and act on proteins. They convert polypeptides to tripeptides, dipeptides and amino acids. It is essential that these enzymes are activated only in the intestine or else they would digest the pancreas.

Peptidases, lipase, maltase, sucrase and lactase are the enzymes present in the **intestinal secretion.**

Action of lipase is the same as the lipase of pancreatic juice.

Sucrase, maltase and lactase complete the remaining digestion of carbohydrates and monosaccharides are finally formed.

Peptidases are activated by enterokinase and polypeptides are converted to smaller peptides and aminoacids.

Thus, digestion of all the nutrients is completed in the small intestine.

It propels the residual, undigested food onwards by peristalsis.

Absorption of nutrients is discussed later on.

9.9 LARGE INTESTINE

The large intestine extends from the end of the ileum to the anus. It is about 1.5 meters long. It surrounds the convolutions of the small intestine.

It is divided into the cecum, colon, rectum and anal canal. Its lumen is larger than that of the small intestine and is largest at its commencement at the cecum. It diminishes gradually till it reaches the rectum. There is a dilatation just above the anal canal. As compared to the small intestine, it is more fixed, more sacculated, and has certain appendages like the appendix. Also, its longitudinal muscular fibers do not form a continuous layer around the gut, but are arranged in three longitudinal bands.

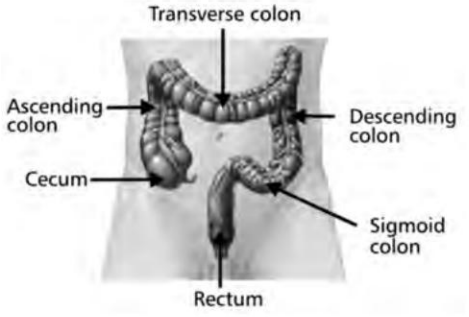


Fig. 9.11 *Large intestine*

The **cecum** starts in the right iliac fossa as a dilated part. The ileum opens at the ileocecal valve which opens in one direction only and thus prevents food to re-enter the ileum. It continues as the ascending colon upwards. It is entirely enveloped by the peritoneum. The **vermiform appendix** is a long, narrow, worm-shaped tube which starts from the apex of the cecum and is closed at the terminal end. It is 4 to 15 cm in length. It usually projects downwards but could pass upward behind the cecum or to the left, behind the ileum and mesentery. It is a vestigial organ and does not perform any function.

The **ascending colon** passes upwards through the right lumbar and hypochondriac regions to the under surface of the liver. Here it turns to the left at the hepatic flexure to form the transverse colon.

The **transverse colon** lies in the epigastric and umbilical regions and passes across the abdominal cavity below and in front of the stomach and duodenum. It goes to the left hypochondriac region below the spleen where it forms the splenic flexure. It then curves downwards and descends down.

The **descending colon** lies in the left lumbar and iliac regions. It goes down into the pelvis.

In the pelvis it forms a bend called the **sigmoid colon** and continues along the posterior wall of the pelvis to the anus.

The **rectum** is about 12 cm long. It starts from the sigmoid colon and ends at the anal canal. Near its termination, it is dilated to form the rectal ampulla.

The **anal canal** starts from the rectum and ends at the anus. It is 2.5 to 4 cm in length. It has no peritoneal covering. There are two sphincters which control the anus—the **internal sphincter** which is under autonomic control and has smooth muscle fibers, and the **external sphincter** which is under voluntary control and has skeletal muscle fibers. It gives a stretch sensation.

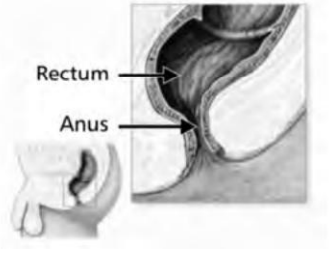


Fig. 9.12 *Anal canal*

9.9.1 Structure

The large intestine has four layers of tissue—serous, muscular, areolar, and mucus.

The **serous (outermost) layer** is derived from the peritoneum. It invests the different portions of the large intestine to a variable extent. The cecum is completely covered by the serous membrane. The ascending and descending colon are covered only in front and at the sides. The transverse colon is completely covered. The rectum is covered on the anterior surface only. The anal canal has no serous covering. The peritoneal covering is thrown into a number of small projections filled with fat. They are numerous on the transverse colon.

The **muscular layer** consists of three long, narrow bands of longitudinal muscle fibers, about one centimeter in width. They are equally spaced around the circumference of the colon and are called **taeniae coli**. Between the thick bands of the taeniae, there is a thin layer of longitudinal muscle fibers. The taeniae stop at the junction of the sigmoid colon and rectum. Between these bands, the intestine bulges out a little.

The **areolar** or **submucosal layer** contains nerves, blood vessels and elastic fiber with collagen, which maintains the shape of the intestine. In this layer there is more lymphoid tissue than in any other part of this system, and this serve the purpose of defense against invading microbes.

Mucosa is made of glandular epithelium. It contains goblet cells which secrete mucus. These cells are absent beyond the junction between the rectum and the anus. It forms folds which are semilunar.

The lining of the anus consists of stratified squamous epithelium which is continuous above with the epithelium of rectum and merges below with the skin beyond the external sphincter. The mucous membrane in the upper part of the anal canal forms folds called anal columns which are 6 to 10 in number.

(a) Arterial Supply It is mainly by the superior and inferior mesenteric arteries.

(b) Venous Drainage It is mainly by the superior and inferior mesenteric veins joining the splenic and gastric veins, which finally join to form the portal vein. Veins draining the distal part of the rectum and the anus drain into the internal iliac veins.

9.9.2 Movements of the Large Intestine

The movements of the large intestine are different. Peristaltic movements which are seen in the other parts of alimentary canal are not seen here. 95% of the contractions of the colon are unsynchronized (nonperistaltic). These contractions mix

the contents of the large intestine back and forth but do not move them forward.

Some contractions are of high amplitude. Propagating contractions occur 6–8 times per day. They are extremely strong contractions. They begin in the first part of the large intestine and sweep around all the way to the rectum and stop there. They move the contents of the large intestine ahead of them and often trigger a bowel movement. These are called **mass movements** and constitute a type of motility not seen elsewhere in the digestive tract. They are also known as **giant migrating contractions**. This movement occurs as soon as food enters the stomach and is called the gastro-colic reflex. This reflex is seen maximally in the morning.

Antiperistaltic contractions also occur which propagate towards the ileum and serve to retard the movement of food through the colon, allowing additional opportunity for absorption of water and electrolytes.

Some circular constrictions also occur at regular distances.

9.9.3 Functions

1. The large intestine's main function is to absorb water from the remaining indigestible food matter and then to pass useless waste material from the body. It absorbs water till a semisolid consistency of feces is achieved. It stores fecal matter in the rectum until it is eliminated through the anus. Thus, it is responsible for eliminating solid waste.
2. Mucus acts as a lubricant and prevents mechanical irritation. It creates an alkaline medium and decreases the acidity of bacterial fermentation.
3. It absorbs vitamins, produced by the bacteria present in the colon. The large intestine has nearly 700 species of bacteria that perform a variety of functions.
   Bacteria produce large amounts of vitamins, especially vitamin K and biotin which are absorbed into the blood. This source of vitamins provides only a small part of the daily requirement, but it contributes considerably when dietary vitamin intake is low. If antibiotics are given that inhibit other species of bacteria as well as the disease-causing bacteria then a person who depends on absorption of vitamins from the large intestine may become vitamin deficient.
4. Undigested polysaccharides are metabolized to short-chain fatty acids and absorbed by passive diffusion. Bicarbonate is secreted which helps to neutralize the increased acidity due to the formation of these fatty acids.
5. Other bacterial products are gas or flatus, which is a mixture of nitrogen and carbon dioxide, with small amounts of hydrogen, methane, and hydrogen sulphide. This is a result of bacterial fermentation of undigested polysaccharides, proteins and fats which gives the typical fecal odour. If these toxic products get absorbed, it could be harmful.
   Absorption of saline, glucose, amino acids and some drugs also take place.
6. Heavy metals are excreted from the blood directly into the colon and passed in feces.
   Mass peristalsis which occurs here pushes the feces towards the rectum.

9.10 PROCESSES IN DIGESTION

1. Mastication

Mastication or chewing is the first mechanical process which takes place when food enters the mouth and is crushed and ground by teeth. Some foods may need to be chewed more and some less. It depends on the consistency of the food. It is the first step of digestion and it increases the surface area of foods to allow more efficient breakdown by enzymes. The teeth chew the food and cut it into small particles. During mastication, the tongue (and to a lesser extent, the lips and cheeks) act to keep food between the grinding surfaces of the teeth. As chewing continues, the food is made softer and warmer and the enzymes in saliva begin to break down carbohydrates in the food. The food thus mixes with the saliva and forms a soft mass called **bolus** which is now swallowed and enters the pharynx. While chewing, the taste of food is appreciated.

Mastication is accomplished through the activity of the four muscles of mastication. They are the masseters, temporals, pterygoids and buccinators. These muscles are supplied by the mandibular division of the trigeminal nerve.

2. Swallowing (deglutition)

Mastication of food takes place in the mouth. A bolus is formed which is ready for being swallowed. This occurs in three stages. The procedure starts voluntarily but is completed reflexly. The bolus moves posteriorly helped by the muscles of the cheek and the tongue. The tongue is pushed against the hard palate leading to positive pressure in the back of the oral cavity. Food now passes into the pharynx.

The bolus, which has entered the pharynx, passes down to the esophagus. Contractions of pharyngeal muscles help push the bolus down. The bolus cannot go back to the mouth because the tongue is pushed up against the hard palate. Re-entry into the pharynx is prevented by the soft palate. The bolus cannot enter into the larynx, because it moves up and forwards and the epiglottis closes it.

Peristaltic waves are initiated and the bolus moves down from the upper esophagus to the lower esophagus with the

peristaltic waves moving downwards. The cardiac sphincter, which is at the mouth of the stomach, relaxes when the bolus comes at the lower end of the esophagus. The bolus enters the stomach. Then the sphincter contracts. This prevents the reflux of the bolus into the esophagus. Mucus in the esophageal wall helps smooth passage of the bolus. The fundus of the stomach forms an acute angle with the esophagus which also prevents reflux of food into the esophagus. The diaphragm is attached to the stomach and its pinching effect also prevents gastric reflux.

3. Digestion

Digestion of food at different levels has been discussed at respective places.

To Summarize Digestion starts in the mouth. Food is broken to small pieces. Amylase converts polysaccharides to disaccharides. Pepsin converts pepsinogen to pepsin; lipase converts fats to fatty acids and glycerol.

Esophagus passes food from the mouth to the stomach.

In the stomach, food mixes with hydrochloric acid (HCl) and digestive enzymes. Mucus lubricates the mucosa and protects the walls from the effect of HCl.

Pepsin converts proteins into simpler substances. Renin aids the digestion of milk proteins, and milk caseinogen is converted into casein, which is digested by pepsin.

Food passes into the small intestine where most nutrients are digested and absorbed.

Bile salts present in **bile** help in emulsification of fat, and big molecules are reduced to smaller ones increasing their surface area. They are then acted upon by lipase (in pancreatic juice and intestinal juice) which converts them to fatty acids and glycerol.

Pancreatic juice contains many enzymes—amylase, lipase, trypsinogen, chymotrypsinogen and procarboxypeptidase.

Amylase converts polysaccharides to disaccharides. Maltose is converted to glucose.

Sucrose is converted to glucose, and fructose and lactose to glucose and galactose.

Enterokinase converts trypsinogen to trypsin, and chymotrypsinogen to chymotrypsin which convert polypeptides to tripeptides, dipeptides and amino acids.

Small Intestine Action of lipase is the same as the lipase of pancreatic juice.

Sucrase, maltase and lactase complete the remaining digestion of carbohydrates and monosaccharides are finally formed.

Peptidases are activated by enterokinase, and polypeptides are converted to smaller peptides and amino acids.

Thus, digestion of all the nutrients is completed in the small intestine.

4. Absorption

Absorption mainly takes place in the stomach, small intestine and large intestine.

Absorption takes place by the mechanism of diffusion, facilitated diffusion or vesicle-mediated transport.

Digested food passes into the blood vessels in the wall of the organs. The small intestine is the site where most of the nutrients from digested food are absorbed.

Absorption in the **stomach** is in a small amount. Some water, certain ions, glucose, some drugs like aspirin, ethanol and vitamin B12 are absorbed from the stomach into the blood.

In the **small intestine,** a majority of the absorption takes place in the jejunum. Fatty acids and glycerol are absorbed from the jejunum and ileum. Water soluble vitamins are absorbed from the small intestine.

Some ions and water are absorbed from the **colon.**

The luminar surface of the ileum is highly convoluted into projections called villi and microvilli; both of which increase the total surface area for absorption. The center of each villus has a single blunt-ended lymphatic vessel called **lacteal** for the absorption of fatty acids and glycerol.

The absorbed materials cross the mucosa into the blood and are carried to other parts of the body either for storage or for further chemical change.

Glucose is carried to the liver where it is stored or used to provide energy for work of the body.

Protein is converted into small molecules and absorbed in the intestine and carried to other parts of the body for construction purpose.

Bile acids combine with the fatty acids and cholesterol and help these molecules to move into the cells of the mucosa. Small molecules are formed back into large molecules, most of which pass into the lymphatics near the intestine. Blood carries the fat to storage depots in the different parts of the body.

Most of the material absorbed is water in which salt is dissolved.

5. Defecation

Defecation means elimination of wastes and undigested food, as feces, from the rectum through the anus. Defecation in infants occurs involuntarily and voluntary control develops in the second or third year.

There is involuntary contraction of the muscles of the rectum and with relaxation of the internal anal sphincter, the process of defecation is initiated. Intra-abdominal pressure increases due to contraction of abdominal muscles and lowering of the diaphragm. This also helps in defecation. If defecation is suppressed then the reflex fades until the next mass reflex.

Feces Feces are a semisolid mass, brown in color due to the presence of stercobilin. It consists of 60 to 70% water, dead and live microbes, fatty acids, mucus, and epithelial cells from the wall of the tract and fiber.

9.11 PANCREAS

The pancreas is a dual-function gland, having features and functions of both endocrine and exocrine glands. It is pale grey in color.

It is 15 cm long and is situated in the epigastric and left hypochondriac region of the abdominal cavity which stretches across the back of the abdomen and lies beneath the stomach. The head of the pancreas is on the right side of the abdomen, located within the curve of the duodenum and is connected to the small intestine at the duodenum. The narrow end of the pancreas, called the tail, extends to the left side of the body.

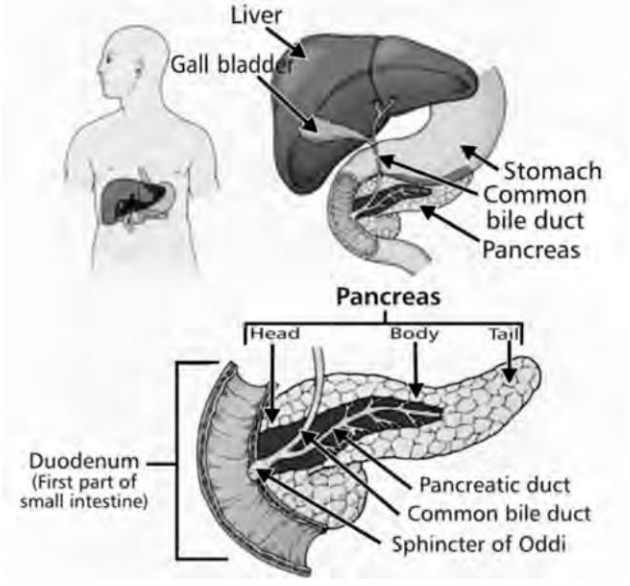


Fig. 9.13 *Pancreas*

The endocrine part of the gland produces several important hormones, including insulin, glucagon, and somatostatin. Details have been discussed in the endocrine section.

The **exocrine part** of the gland consists of lobules which are made of small alveoli. Secretory cells are located in the walls of the alveoli. A small duct drains from the lobule and these ducts unite to form the pancreatic duct. This passes along the entire gland and opens into the duodenum. Before opening into the duodenum, it joins the common bile duct to form the **pancreatic ampulla**. Here, there is a sphincter which controls the opening of the ampulla. This part secretes pancreatic juice containing digestive enzymes that pass to the small intestine. These enzymes are designed to digest foods and help neutralize chyme and break down proteins, fats and starch.

Chyme contains partly digested food that is passed from the stomach to the duodenum. If the pancreas is not working properly to neutralize chyme and break down proteins, fats and starch, starvation may occur.

(a) Arterial Supply It is by splenic and mesenteric arteries.

(b) Venous Drainage Venous blood drains into splenic and mesenteric veins which join other veins to form the portal vein.

9.12 LIVER

The liver is a soft, pinkish-brown triangular organ and is, both, the largest internal organ and the largest gland in the human body, except for the skin. It lies in the upper abdomen, resting just below the diaphragm and occupies the right hypochondriac region, some part of the epigastric region and extends into the left hypochondriac region.

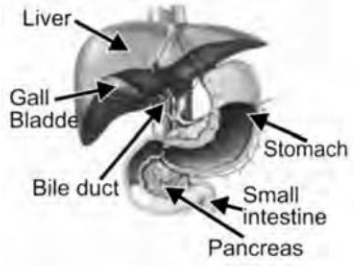


Fig. 9.14 *Liver*

It aids in digestion and removes waste products and worn-out cells from the blood. It weighs about 1.5 to 2.3 kilograms. It measures about 20 cm across and 17 cm vertically, and is 12 cm thick.

9.12.1 Relations

It lies to the right of the stomach and overlies the gall bladder.

It rests just below the diaphragm.

Posteriorly are the esophagus, inferior vena cava, vertebral column and diaphragm.

Inferiorly are the duodenum, stomach, bile duct, right kidney, adrenals and hepatic flexure of the colon.

9.12.2 Lobes

Each lobe is made up of units called **lobules**. There are between 50,000 and 100,000 lobules in the liver. Each lobule consists of a central vein surrounded by tiny liver cells grouped in sheets or bundles. These cells carry out various functions of the liver. Cavities known as **sinusoids** separate the groups of cells within a lobule. The sinusoids give the liver a spongy texture and enable it to hold large amounts of blood.

Blood drains from the sinusoids into the central vein which then joins the hepatic vein to carry blood out from the liver. It empties into the inferior vena cava.

On the surface of the lobules there are ducts, veins and arteries that carry fluids to and from them.

The liver is divided into four lobes. There are two main lobes—the right lobe, which is larger, and the left lobe. The **falciform ligament** which is visible on the front of the liver divides these two lobes.

From behind, two additional lobes can be seen. These are the **caudate lobe** and the **quadrate lobe**. The **transverse fissure** (or **porta hepatis**) separates the caudate from the quadrate lobe. The lobes are divided up by the **ligamentum venosum** and **ligamentum teres**.

The liver is entirely covered by the visceral peritoneum except where it is in connection with the diaphragm, called the bare area. The peritoneum reduces friction with other organs. It also folds back on itself to form the falciform ligament and the right and left triangular ligaments.

The ligaments of the liver are different from the true anatomic ligaments in joints.

On the posterior surface of the liver, there is a region where structures enter and leave the liver. This is called the **portal fissure**. The portal vein collects blood from the stomach, spleen, pancreas and large and small intestine and enters the liver. The hepatic artery enters through this fissure. The right and left hepatic ducts leave and carry bile to the gall bladder. Sympathetic and parasympathetic nerve fibers enter here. The lymph vessels leave here.

9.12.3 Functions

The liver has a very important role to play in the body. It synthesizes, stores, excretes, secretes, metabolizes, detoxicates and generates different substances.

It synthesizes bile which contains bile salts, bile pigments and cholesterol.

1. Carbohydrate Metabolism

It metabolizes and stores carbohydrates. In the presence of insulin, it converts glucose to glycogen and back to glucose in the presence of glucagon. Thus, blood-glucose level is maintained.

During hypoglycemia, glycogenesis and glycogenolysis takes place in the liver.

It also carries out neoglycogenesis—glycogen formation from sources other than carbohydrates like proteins and fats.

Fat synthesis from carbohydrates also takes place.

2. Protein Metabolism

The main function is de-amination of amino acids. It removes nitrogenous portion from amino acids and forms urea which is excreted in urine.

It synthesizes proteins, including albumin, plasma proteins and most of the blood-clotting factors from available amino acids.

Formation of urea and uric acid takes place in the liver.

Heat is generated by specific dynamic action of proteins.

3. Fat Metabolism

Desaturation of fats takes place in the liver. It synthesizes, stores and metabolizes fats, fatty acids and cholesterol.

Fats are also synthesized from proteins and carbohydrates.

Ketones are formed in the liver.

Bile contains bile acids which help the intestinal absorption of fats and the fat-soluble vitamins A, D, E, and K and stores them.

Bilirubin is produced from the breakdown of old red blood cells and ammonia is produced from the breakdown of proteins. The liver metabolizes these substances and helps in eliminating them.

The liver detoxifies drugs, alcohol, and environmental toxins by metabolizing and/or removing them.

The macrophages present among the cells lining the sinusoids, ingest and destroy foreign particles present in the blood.

Iron, B12, riboflavin, pyridoxine and folic acid are stored in the liver and released when required and transferred to bone marrow.

Heparin is synthesized from the mast cells of the liver and released into the blood as an anticoagulant to prevent intravascular coagulation of blood.

It inactivates hormones like insulin, cortisol, thyroid, sex hormones, glucagon and aldosterone.

The liver has a high metabolic rate and generates a great deal of heat. It is the main heat-producing organ of the body.

Toxic metals and microbes and their toxins are excreted in the bile.

Kupfer cells are reticulo-endothelial cells manufactured in the liver. They protect the body against microbes by processes like agglutination, bacteriolysis, phagocytosis and precipitation.

9.13 BILIARY TRACT

The biliary tract consists of channels and ducts that convey bile from the liver into the lumen of the small intestine. Hepatocytes are arranged in plates with their apical surfaces facing and surrounding the sinusoids. The surfaces of adjoining hepatocytes are joined together by junctional complexes to form canaliculi which are the first channels in the biliary system. A bile canaliculus is not a duct, but a dilated space between adjacent hepatocytes.

Hepatocytes secrete bile into the canaliculi. The flow of bile is in a direction opposite to the direction of the blood flow. From the canaliculi, bile flows into bile ducts. Bile ducts lie in close proximity to the terminal branches of the portal vein and hepatic artery. The grouping of bile duct, hepatic arteriole and portal venule is called the portal triad.

The hepatic ducts join to form the common bile duct and this is joined by the cystic duct of the gall bladder after traveling 3 cm. The cystic and hepatic ducts form the common bile duct which passes behind the head of the pancreas and joins the main pancreatic duct at hepatopancreatic ampulla and opens into the duodenum. The opening is controlled by the **sphincter of Oddi**.

9.14 GALL BLADDER

The gall bladder is a hollow pear-shaped organ on the posterior surface of the liver and is attached to it with connective tissue. It lies in the concavity of the liver known as the **gall bladder fossa**. The gall bladder is divided into three parts—fundus, body, and neck. The neck tapers and is continuous with the cystic duct.

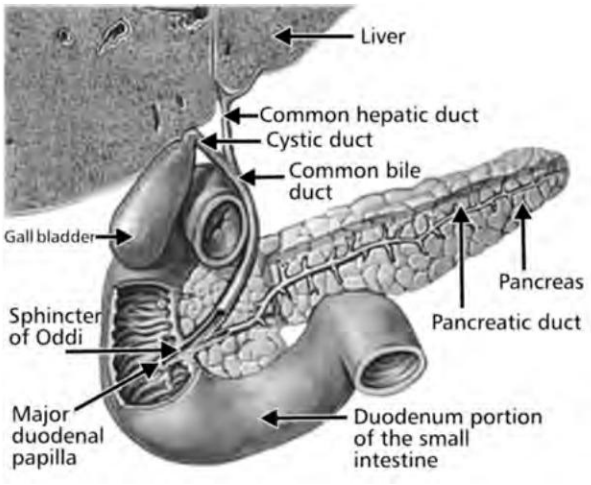


Fig. 9.15 *Gall bladder*

It concentrates bile produced in the liver.

It has a simple columnar epithelial lining with recesses called **Aschoff's recesses**, which are pouches inside the lining.

Under the epithelium, there is a layer of connective tissue beneath which is a wall of smooth muscle called **muscularis externa**. The muscular layer contracts in response to **cholecystokinin**, a hormone secreted by the duodenum.

The peritoneum covers only the inferior surface and holds it in its place.

(a) Arterial Supply The arterial supply is by the cystic artery, a branch of the hepatic artery.

(b) Venous Drainage Blood is drained by the cystic vein which joins the portal vein.

(c) Nerve Supply It has both sympathetic and parasympathetic supply.

9.14.1 Functions

The gall bladder stores about 50 mL of bile. When food containing fat enters the digestive tract, it stimulates the secretion of cholecystokinin, and bile is released into the duodenum.

It concentrates bile and helps in absorption of water and inorganic salts.

It secretes mucus and excretes cholesterol.

Pressure is maintained in the billiary tract by the gall bladder.

9.14.2 Bile

Bile is a secretory and excretory product of the liver. It enters the duodenum only after ingestion of food.

After being stored in the gall bladder, the bile becomes more concentrated, its potency is increased and its effect on fats is intensified.

It is a complex fluid, containing water, electrolytes and organic molecules like bile salts, bile pigments, cholesterol and phospholipids. It contains no enzymes.

Bile salts are sodium taurocholate and sodium glycocolate, which are synthesized in the liver. They carry bilirubin and biliverdin to the gall bladder.

400 to 800 mL of bile is secreted daily.

Functions

1. Bile emulsifies fats into smaller droplets. Emulsification is not digestion, but it increases the surface area of fat, making it available for digestion by lipases, which cannot access the inside of lipid droplets.
2. Bile acid helps digestion and absorption of fats and hence helps absorption of fat-soluble vitamins in the small intestine.
3. The alkaline bile neutralizes any excess stomach acid before it enters the ileum.
4. Bile salts act as bactericides, destroying microbes that may be present in the food.
5. It serves as the route of excretion for bilirubin (derived from hemoglobin by glucuronidation), a by-product of red blood cells recycled by the liver. It is secreted into bile and excreted in feces.
6. It contains mucus which acts as a buffer.

7. Bile has a laxative action. It stimulates peristalsis.
8. Bile stimulates billiary secretion, known as **cholagogue action**.
9. Certain heavy metals, bacteria, toxins lecithin and cholesterol are excreted in bile.
10. Bile stimulates secretin, which stimulates biliary, pancreatic and intestinal secretions.

9.15 DISORDERS OF DIGESTIVE SYSTEM

1. Nausea

Nausea is an uncomfortable feeling which occurs with or precedes vomiting. Nausea is the body's way of reacting to an infection or any condition. Its cause could be local like digestive disorders (gastroenteritis, peptic ulcer, colitis, gall stones) or general (pregnancy, vertigo, emotional disorders).

2. Anorexia

Anorexia means loss of appetite. It is an eating disorder resulting from local or general causes. It is seen more in young people around puberty. It is also seen in anxiety or depression.

3. Vomiting (emesis)

Vomiting is the forceful expulsion of the contents of one's stomach through the mouth. It could result from central causes like brain tumors, or local causes like gastritis or general causes like poisoning.

4. Diarrhea

Diarrhea is an increased frequency in stool, as compared to the normal amount of stool passed. It is primarily due to increased intestinal motility. Hence less time is available for absorption and more fluid is passed with feces.

Pathophysiology of Nausea, Vomiting, Diarrhea, Anorexia It is often said that the exact cause of these disorders is yet to be identified. It could be due to infection, viral or bacterial, or could be due to some allergy, side effects of antibiotics, intestinal disease or functional disorder.

5. Constipation

Constipation is defined as having bowel movement, fewer than three times a week and passage of small amounts of hard, dry stool which is difficult to evacuate. Some people who are constipated find it difficult to have a bowel movement and experience straining, bloating and the sensation of a full bowel.

Pathophysiology When the colon's muscle contractions are slow or sluggish, the stool moves very slowly, resulting in too much water being absorbed. It can occur in irritable bowel syndrome, change in lifestyle, abuse of laxatives, lack of exercise, medications, not enough fiber in diet or not enough fluids taken.

6. Dysphagia

Dysphagia means difficulty in swallowing. There may be complete dysphagia or it may be to solid or liquids.

Pathophysiology Dysphagia occurs when there is a problem with any part of the swallowing process. It could be due to weak tongue or cheek muscles.

It could occur due to some local condition in the pharynx or larynx or esophagus. It could also occur due to pressure from outside on the esophagus (lymph nodes or enlarged thymus). An infection or irritation of the esophagus can cause dysphagia.

It could occur due to inability to start the swallowing reflex due to some neurological condition like stroke or Parkinsonism. In these cases, muscle movements are not initiated and so food cannot move from mouth to stomach. Muscles are damaged or weakened.

People born with abnormalities of the swallowing mechanism can also develop dysphagia.

7. Flatulence

Flatulence is the state of having excessive gas in the stomach or intestine. This can result in an uncomfortable feeling of bloating and also increased belching or passing gas from the rectum.

Pathophysiology It can occur due to aerophagy, as a by-product of the digestion process, intestinal fermentation, and incomplete digestion or due to constipation.

8. Heartburn

Heartburn is an uncomfortable burning sensation felt at the upper part of the esophagus. There is a sour burning sensation behind the upper part of the sternum.

Pathophysiology It is due to gastric flow from the stomach into the esophagus in the form of regurgitation.

9. Gastritis

Gastritis is an inflammation of the stomach mucosa.

Pathophysiology The lining of the stomach is quite strong and can withstand strong acid or trauma. A number of conditions can still lead to irritation and inflammation of the mucosa—spicy food, too much alcohol, smoking, prolonged

use of nonsteroidal anti-inflammatory drugs, traumatic injury or burns, major surgery, infection with *E. coli* or salmonella and certain disease like auto-immune disorders and chronic bile reflux.

10. Gastroenteritis

Gastroenteritis is a condition caused by irritation and inflammation of the stomach and the small intestine. There is diarrhea, crampy abdominal pain, nausea, anorexia and vomiting.

Pathophysiology Viral infection is the most common cause. It can also be due to bacterial, parasitic or fungal infection. It can be transferred by contact with contaminated food and water. It can also be part of an adverse reaction to something in the diet or medication.

11. Peptic Ulcer

Peptic ulcer is an area where the tissue has been destroyed or eroded. They are open sores. They can develop in the esophagus (esophageal ulcer) or in the stomach (gastric ulcer) or in the intestine (intestinal ulcer). The most common symptom is pain.

Pathophysiology The mucus membrane lining is eroded or corroded by the acidic digestive juices secreted by the stomach cells and there is breakdown of tissue.

Actually, excess acid was believed to be the major cause. Acid is still considered significant in ulcer formation, but it has been found that infection of the stomach by bacteria called *Helicobacter pyloricus* (*H. pylori*) is responsible for ulcer formation.

Use of nonsteroidal anti-inflammatory drugs can cause ulcers.

Cigarette smoking is another cause.

A disturbed mind produces excessive vagal activity resulting in more acid secretion.

Irritants, and spicy food can also damage the mucosa.

12. Cholecystitis

Cholecystitis is defined as inflammation of the gall bladder.

Pathophysiology Most commonly it occurs due to obstruction of the cystic duct from cholelithiasis. 90% of patients have stones in the cystic duct. Remaining 10% are acalculous cholecystitis.

In calculus cholecystitis, obstruction of the cystic duct causes distension of the gall bladder. Blood flow and lymphatic drainage get affected. There is mucosal ischemia and necrosis. The response to cholecystokinin is abolished by endotoxins. There is gall-bladder stasis.

The exact mechanism in acalculous cholecystitis is not clear. It follows major surgery, severe trauma, sepsis, debilitation and prolonged fasting. Some theories have been put forward.

It may result from retained bile which acts as a noxious substance.

With prolonged fasting, the gall bladder does not receive cholecystokinin stimulus to empty; hence, concentrated bile remains stagnant in the lumen.

Other causes for acalculous cholecystitis are diabetes mellitus, cardiac disease, salmonella infection, sickle-cell disease or microsporidiosis in patients with AIDS. The mechanism, again, is not clear.

13. Appendicitis

Appendicitis is an inflammation of the appendix, a vestigial structure extending from the cecum at the ileo-cecal junction. The exact function of this structure is not certain. Acute appendicitis is a medical emergency. An inflamed appendix could burst or perforate leading to peritonitis and if left untreated, could become fatal.

Pathophysiology Appendicitis occurs when it gets blocked, often by stool, a foreign body, or cancer. Infection can also cause blockage, as the mucosa swells up in response to infection.

14. Peritonitis

Peritonitis is an inflammation of the visceral and parietal peritoneum. It could be localized or generalized. It is usually treated by surgery.

Pathophysiology Peritonitis may occur due to infection or from non-infectious process.

Infected Peritonitis Infected peritonitis could occur due to perforation of an abdominal organ like the stomach (peptic ulcer), duodenum (ulcer) or intestine (appendicitis, inflammatory bowel disease).

It could occur due to disruption of the peritoneum, even in the absence of perforation of an organ—surgical wound, trauma.

It can occur with intra-peritoneal dialysis.

Spontaneous bacterial peritonitis can occur even in the absence of any source of contamination—ascites, especially in children.

Systemic infections like tuberculosis can also lead to peritonitis.

Non-infected Peritonitis It can occur due to leakage of sterile body fluids into the peritoneum such as blood (trauma), gastric juice (peptic ulcer), bile (liver biopsy), pancreatic juice (pancreatitis), or urine (trauma).

Sterile abdominal surgery causes localized or minimal generalized peritonitis.

15. Hepatitis

Hepatitis is an inflammation of the liver characterized by the presence of inflammation of the cells, followed by diffuse or patchy necrosis of the hepatic cells.

Acute hepatitis may start, flare up and resolve quickly. Chronic hepatitis may persist for many years, and lead to liver damage followed by liver failure, cirrhosis or terminate in cancer.

Pathophysiology Hepatitis is most commonly caused by a virus. There are mainly three viruses—hepatitis A virus, hepatitis B virus and hepatitis C virus.

In rare cases, the **Epstein Barr virus** can also cause hepatitis because it causes inflammation of the liver.

Other viruses and bacteria that can cause hepatitis are hepatitis D and E, and cytomegalovirus.

It can also be caused by drugs (acetaminophen), chemicals, poisonous mushrooms or alcohol.

Inherited diseases and auto-immune disease (immune cells attack the liver and cause auto-immune hepatitis) can also cause hepatitis.

16. Fatty Liver

Fatty liver is the formation of large vacuoles of triglyceride fat in the liver cells via the process of steatosis—abnormal retention of lipid in the cells.

Pathophysiology Fatty liver is seen with excessive alcohol intake. It is seen more in obese people.

It is seen in diseases which affect fat metabolism and also in metabolic disorders like diabetes, hypertension and dyslipidemia.

It occurs with malnutrition, weight loss, jejuno-ileal bypass and bacterial overgrowth where the cause is chiefly nutritional deficiency.

Certain drugs and toxins also cause fatty liver—amiodorone, glucocorticoids, methotraxate.

17. Cirrhosis of Liver

Cirrhosis of liver is a complication of many liver diseases. There is abnormal structure and function of the liver. The liver slowly deteriorates.

Pathophysiology There is chronic injury and the liver cells gradually die, and the inflammation and repair associated with the dying liver cells causes scar tissue to form. Hence healthy liver tissue gets replaced, sinusoids get blocked and there is blockage of flow of blood. Those cells which do not die multiply in an attempt to replace the cells that have died. There is formation of clusters of newly formed liver cells forming regenerating nodules.

The conditions which lead to cirrhosis are heavy alcohol consumption, chronic hepatitis C infection, chemicals, viruses, toxic metals (iron or copper in genetic diseases) and auto-immune liver disease, where the body's immune system attacks the liver.

18. Jaundice

Jaundice, also known as **icterus**, is the yellowish discoloration of the skin, the conjunctival membrane over the sclera, and other mucus membranes.

It is actually not a disease but a sign that occurs in many diseases.

Pathophysiology When red blood cells get old, they are destroyed. Hemoglobin is released from the destroyed cells after the iron it contains is removed. The chemical that remains in the blood now becomes bilirubin. Jaundice is caused by increased levels of this bilirubin. The concentration of bilirubin in plasma should be more than 1.5 mg/dL, three times the normal value for the yellowish discoloration to be visible.

Jaundice occurs when there is more production of bilirubin than the liver can remove—hemolytic anemia—pre-hepatic jaundice. It can occur when due to some defect in the liver the bilirubin is not removed from the blood—hepatic jaundice. It can occur due to blockage of the bile ducts that decreases the flow of bile and bilirubin from the liver into the intestines—obstructive jaundice.

REVIEW QUESTIONS

1. Describe general anatomical structure of the digestive system.
2. Describe the anatomy of oral cavity.
3. Describe salivary glands and their functions.
4. Write a note on the anatomy, blood supply and functions of the stomach.
5. Write a note on the structure and functions of the small intestine. Explain its movements.
6. Discuss structure, movements and functions of the large intestine.
7. Write a note on the anatomy of the gall bladder and biliary apparatus.
8. Write a note on gastric juice and different phases of gastric-acid secretion.
9. What is digestion and absorption? Discuss digestion of proteins, carbohydrates and fat.

10. Discuss in brief the disorders of the alimentary system.
11. Write a note on enzymes involved in digestion.
12. Write short notes on:
    a. Mastication
    b. Swallowing
    c. Defecation
    d. Pancreas
    e. Liver
    f. Peristalsis
    g. Esophagus
    h. G I hormones
    i. Functions of saliva
    j. Functions of bile
    k Jaundice

Chapter

10 Nervous System

- **ANATOMY**
  - **Central nervous system**
    - **Brain**
    - **Spinal cord**
  - **Peripheral nervous system**
    - **Motor**
    - **Sensory**
    - **Mixed**
    - **Cranial nerves**
    - **Spinal nerves**
      - **Cervical plexus**
      - **Brachial plexus**
      - **Lumbar plexus**
      - **Sacral plexus**
    - **Brain**
      - **Cerebrum**
        - Motor area
        - Sensory area
      - **Internal capsule**
      - **Other area of the cerebrum**
        - Basal ganglia
        - Thalamus
        - Hypothalamus
    - **Brain stem**
      - **Midbrain**
      - **Pons**
      - **Medulla oblongata**
      - **Reticular activating system**
    - **Limbic system**
    - **Cerebellum**
      - **Functions**
      - **Disorders**
    - **Extrapyramidal system**
      - **Basal ganglia**
    - **Meninges**
      - **Dura mater**
      - **Arachnoid mater**
      - **Pia mater**
    - **CSF**
    - **Ventricles of the brain**
    - **Blood–brain barrier**

- Spinal cord
  - External structure
  - Internal structure
- Autonomic nervous system
  - External Sympathetic
    - Functions
  - Parasympathetic
    - Functions

• PHYSIOLOGY

- Neurons
  - Action potential
  - Transmission of nerve impulse
  - Excitation
    - Conduction coupling process
  - Neuromuscular junction
- Synapse
  - Classification
    - Functional, anatomic
  - Functions
- Reflex action
  - Classification
    - First, second, third, fourth
- Sensation
  - Classification
    - Somatic sense, special sense
- Receptors
  - Exteroreceptors
  - Interoreceptors
  - Proprioceptors
  - Classification
    - Somatic sense special sense
  - Histological classification
    - Uncapsulated receptors
    - capsulated receptor
  - Properties of receptors
    - Specificity of response
    - Adaptation
    - Response to increase in strength of stimulus
    - Receptor potential
    - Control of Receptor
    - Recruitment
    - Inhibition
- EEG
  - Clinical application
  - Procedure
- Sleep
  - Stages of sleep
  - Benefits of sleep
  - Drugs and sleep
  - Dreaming
  - Sleep and Disease
  - Sleep Disorders

- Speech
- Neurotransmitters
  - Types
    - Excitatory neurotransmitters
    - Inhibitory neurotransmitters
  - Functional Significance

- **DISORDERS**
  - Dementia
  - Alzheimer's disease
  - Schizophrenia
  - Anxiety
  - Depression
  - Parkinson's disease
  - Infections
    - Meningitis
    - Encephelitis
    - Poliomyelitis
    - Myelitis
  - Peripheral neuropathy
  - Cerebrovascular disease

Introduction

The nervous system is a highly organized system. It consists of a network of specialized cells that communicate information about the individuals surroundings to the brain and spinal cord. It receives, stores, releases and processes information, and causes responses in other parts of the body, affecting other physiological functions. It controls all other systems mediating through the cell, tissue and organs. It helps to maintain internal environment of the body.

10.1 ANATOMY

The nervous system is composed of neurons and other specialized cells, called **glia**, that aid in the function of the neurons. The unique feature of this system is that, once destroyed, due to disease or injury, it cannot regenerate. Hence, once injured, both the brain and the spinal cord are permanently damaged.

The nervous system is divided broadly into two categories:

1. Central nervous system
2. Peripheral nervous system

Neurons generate and conduct impulses between and within the two systems.

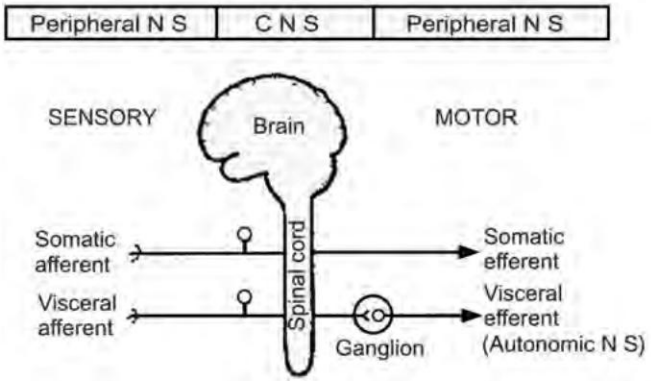


Fig. 10.1 *Organisation of the nervous system*

Functionally, it is divided into voluntary or somatic nervous system, and autonomic or involuntary or visceral nervous system.

The somatic nervous system is responsible for coordinating voluntary body movements (i.e., activities that are under conscious control). The autonomic nervous system is responsible for coordinating involuntary functions, such as breathing, blood pressure and digestion.

These divisions of the nervous system can be further divided according to the direction in which they conduct nerve impulses:

1. **Afferent system** (by sensory neurons), which carry impulses from a somatic receptor to the CNS
2. **Efferent system** (by motor neurons), which carry impulses from the CNS to an effector organ

The relay system by interneurons (also called 'relay neurons') transmit impulses between the sensory and motor neurons (both in the CNS and PNS).

10.1.1 Central Nervous System (CNS)

The central nervous system is the largest part of the nervous system. It includes the brain and spinal cord. The skull contains and protects the brain, while the spinal canal of the vertebral column holds and protects the spinal cord. The CNS is covered by the meninges, a three-layered protective coat.

1. Brain

The brain consists of the cerebral cortex, cerebellum, thalamus, hypothalamus, basal ganglia, limbic system and reticular formation.

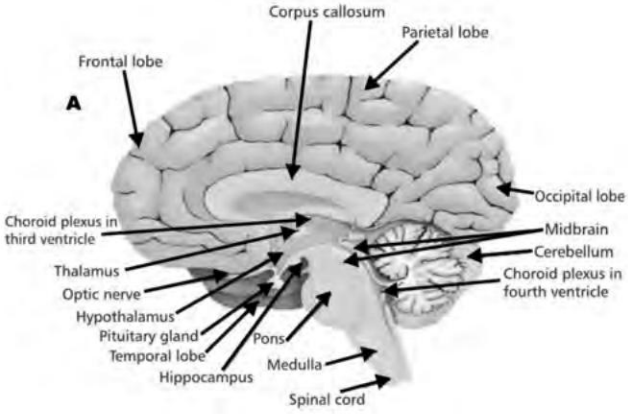


Fig. 10.2 *Brain—Sagittal section*

The brain stem consists of three parts—upper part (the midbrain) middle part (the pons) and lower part (the medulla oblongata).

2. Spinal Cord

The brain stem continues downwards as the spinal cord.

It begins from the foramen magnum and ends at the level of the 1st lumbar vertebra.

10.1.2 Peripheral Nervous System (PNS)

According to functions performed; the peripheral system consists of the following:

(i) Motor System In which impulses go from the central nervous system to the peripheral nervous system

(ii) Sensory System In which impulses go from the peripheral nervous system to the central nervous system

(iii) Mixed System According to the origin, the peripheral system consists of

1. Cranial nerves which are 12 in number and they originate from the brain tissue.
2. Spinal nerves which originate from the spinal cord and there are 31 pairs of spinal nerves

1. Cranial Nerves

Cranial nerves emerge directly from the brain stem. There are 12 pairs of cranial nerves. They originate from nuclei of the inferior surface of the brain—some are sensory, some are motor and some are mixed.

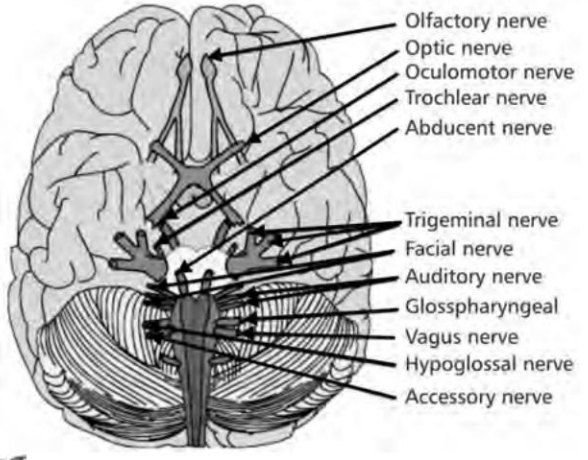


Fig. 10.3 *Origin of cranial nerves (Refer colour figure)*

(a) 1st Cranial Nerve—Olfactory Nerve (Sensory Nerve)

The olfactory nerve carries out the function of perceiving the sense of smell.

It is composed of the rootlets of olfactory hair cells in the nasal mucosa and is not visible on the ventral surface of the brain. The rootlets end in the olfactory bulb. The olfactory tract contains nerve fibers projecting out of the olfactory bulb to the brain, in the temporal lobe of the cerebrum, which is the area of perception of smell.

To test the function of the olfactory nerve, block one of the patient's nostrils and bring a familiar substance, e.g., soap or coffee under the open nostril. The test is then repeated on the other nostril. Other substances are then used in the same way.

For further details, refer to the chapter on special senses.

(b) 2nd Cranial Nerve—Optic Nerve (Sensory Nerve)

They are nerves of sense of sight (vision).

It is composed of retinal ganglion cell axons. It leaves the orbit (eye) via the optic canal, running postero-medially towards the optic chiasma, where there is a partial decussation (crossing) of fibers from the nasal visual fields of both eyes. Most of the axons of the optic nerve terminate in the lateral geniculate nucleus of thalamus. From the lateral geniculate body, fibers of the optic radiation pass to the visual cortex in the occipital lobe of the brain, which is the center for sight.

From the thalamus, some fibers, also, go to the cerebellum. These fibers carry impulses from the eye to maintain balance, posture and orientation of the head in space.

The central retinal artery and vein are enclosed along with the fibers of the optic nerve.

For further details, refer to the chapter on special senses.

(c) 3rd Cranial Nerve—Oculomotor Nerve (Motor Nerve)

The oculomotor nerve arises from nerve cells near the cerebral aqueduct. The muscles it controls are the striated muscles, viz., levator palpebrae superioris and extraocular muscles—superior, medial and inferior recti and inferior oblique.

The Edinger–Westphal nucleus supply parasympathetic fibers to the eye via the ciliary ganglion, and thus controls the sphincter pupillae muscle (affecting pupil constriction) and the ciliary muscle (affecting accommodation).

It controls most of the eye's movements, constriction of the pupil, and keeps the eyelid open. (IV and VI cranial nerves also participate in control of eye movements.)

Cranial nerves III, IV and VI are usually tested together. The patient holds his head still and follows (only with the eyes) a finger or penlight that moves in various directions, in front of him. By observing the eye movements and eyelids, information about the extraocular muscles, the levator palpebrae superioris muscle, and thus, cranial nerves III, IV, and VI can be tested.

(d) 4th Cranial Nerve—Trochlear Nerve (Motor Nerve)

It is a motor nerve that innervates a single muscle, the superior oblique muscle of the eye. It is unique among the cranial nerves in several respects. It is the smallest nerve in terms of the number of axons it contains. Along with the optic nerve (cranial nerve II), it is the only cranial nerve that decussates (crosses to the other side) before innervating its target. Finally, it is the only cranial nerve that exits from the dorsal aspect of the brain stem.

(e) 5th Cranial Nerve—Trigeminal Nerve (Mixed Nerve)

It is primarily a sensory nerve, but it also has certain motor functions (biting and chewing). It is the largest of the cranial nerves. It has three major branches. It is the chief sensory nerve for the head and face, oral cavity, nasal cavity and teeth. It receives impulses of pain, touch and temperature from these areas. Motor fibers innervate muscles of mastication.

The trigeminal nerve has 3 main branches—ophthalmic branch, maxillary branch and the mandibular branch.

The **ophthalmic branch** is sensory and supplies the conjunctiva of the eye, lacrimal glands, eyelids, anterior aspect of scalp, forehead and mucus membrane of the nose.

The **maxillary branch** is sensory and supplies upper eyelids, upper gums and upper teeth, and the cheeks.

The **mandibular branch** is both motor and sensory and is the largest of the 3 divisions. It supplies the teeth, gums of lower jaw, pinna of the ear, lower lip and tongue.

The motor fibers supply the muscles of mastication.

The sensory component is tested for touch and pain using cotton and a pin.

Motor function is tested by asking the person to clench his teeth and to move the jaw from side to side.

(f) 6th Cranial Nerve—Abducent Nerve (Motor Nerve) It controls the movement of a single muscle, the lateral rectus muscle, that moves the eye outwards. It arises from a group of cells, lying under the floor of the 4th ventricle. Intracranially it has the longest route compared to all the other cranial nerves.

(g) 7th Cranial Nerve—Facial Nerve (Mixed Nerve) It emerges from the brain stem, between the pons and the medulla. It controls the muscles of facial expression and carries the taste sensation from the anterior two thirds of the tongue. It also supplies preganglionic parasympathetic fibers to several head and neck ganglia.

Its main function is motor control of most of the muscles of facial expression. It also innervates the posterior belly of the digastric muscle, the stylohyoid muscle, and the stapedius muscle of the middle ear.

The facial nerve also supplies parasympathetic fibers to the submandibular gland and sublingual glands via chorda tympani. Parasympathetic innervation serves to increase the flow of saliva from these glands. It also supplies parasympathetic innervation to the nasal mucosa and the lacrimal gland via the pterygopalatine ganglion.

The facial nerve also functions as the efferent limb of the corneal reflex.

Voluntary facial movements, such as wrinkling the forehead, frowning movement of the eyebrows, closing the eyes tightly, pursing the lips, puffing out the cheeks and showing teeth, all test the facial nerve. There should be no noticeable asymmetry of the face at rest or on facial movements.

Taste can be tested on the anterior 2/3 of the tongue. This can be tested with a swab dipped in a flavored solution, e.g., sugar, salt, etc.

(h) 8th Cranial Nerve—Vestibulocochlear Nerve (Sensory and Auditory) The vestibulocochlear nerve (also known as the auditory or acoustic nerve) is responsible for transmitting sound and equilibrium (balance) information from the inner ear to the brain.

The vestibulocochlear nerve has 2 sets of fibers.

The vestibular nerve arises from semicircular canals of the inner ear. It conveys impulses to the cerebellum and maintains balance and posture.

The cochlear nerve takes its origin in the organ of corti in the inner ear. It conveys impulses to hearing—auditory areas in cerebral cortex, where sound is perceived.

It is, thus, the nerve for hearing and maintaining balance and posture.

Hearing is tested by holding a wristwatch near the ear on both the sides alternately.

For further details refer to the chapter on special senses.

(i) 9th Cranial Nerve—Glossopharyngeal Nerve (Mixed Nerve) It arises from the nuclei in the medulla oblongata. It comes out from the brain stem, from the sides of the upper medulla, near the vagus nerve.

It receives sensory fibers from the posterior one third of the tongue, the tonsils, the pharynx, the middle ear and the carotid sinus.

It supplies parasympathetic fibers to the parotid glands via the otic ganglion.

It supplies motor fibers to stylopharyngeus muscle.

It contributes to the pharyngeal plexus.

It is responsible for swallowing (deglutition) and the gag reflex.

It is tested by carrying out the gag reflex. Taste is tested with a swab dipped in a flavored solution, and putting it on the posterior aspect of the tongue.

(j) 10th Cranial Nerve—Vagus Nerve (Mixed Nerve) It starts from the brain stem (within the medulla oblongata) and extends, through the jugular foramen, down below the head, to the neck, chest and abdomen, where it contributes to the innervation of the viscera. Besides output to the various organs in the body, the vagus nerve conveys sensory information about the state of the body's organs to the central nervous system. 80–90% of the nerve fibers in the vagus nerve are afferent (sensory) nerves giving information regarding the state of the viscera to the brain.

The vagus nerve forms a very important part of the parasympathetic nervous system.

It has both motor and sensory fibers.

The vagus nerve supplies motor parasympathetic fibers to all the organs, except the suprarenal (adrenal) glands, from the neck down to the second segment of the transverse colon.

Sensory fibers convey impulses from the lining of all these structures and carry them to the brain.

Thus, the vagus nerve is responsible for heart rate, gastrointestinal peristalsis, sweating, and a few muscle movements in the mouth, including speech (via the recurrent laryngeal nerve) and keeping the larynx open for breathing. It also receives

some sensation from the outer ear, via the auricular branch and part of the meninges.

Extracranially, it is the longest of the cranial nerves.

(k) 11th Cranial Nerve—Accessory Nerve (Motor Nerve)

It emerges from the skull and receives an additional (accessory) root from the upper part of the spinal cord, and hence the name. It arises from cell bodies in the medulla oblongata and spinal cord and supplies the sternocleidomastoid and trapezius muscles. The sternocleidomastoid muscle is in the front of the neck and its function is to turn the head. The trapezius muscle moves the scapula (shrugging of shoulders) and helps to pull the head back. Some branches join the vagus nerve to supply pharyngeal and laryngeal muscles.

The nerve can be tested by asking the patient to shrug his shoulders (trapezius) and turn the face from side to side (sternomastoids).

(l) 12th Cranial Nerve—Hypoglossal Nerve (Motor Nerve)

The hypoglossal nerve is the nerve leading to the tongue. The nerve arises from the hypoglossal nucleus and emerges from the medulla oblongata.

It supplies motor fibers to all of the muscles of the tongue, except the palatoglossus muscle and muscles surrounding the hyoid bone. It helps in swallowing and speech.

To test the function of the nerve, the patient is asked to poke out his tongue. If there is a loss of function on one side (unilateral paralysis), the tongue will point towards the affected side.

The strength of the tongue can be tested by getting the person to poke the inside of the cheek, and feeling how strongly a finger can be pushed against the cheek from outside.

The tongue should be looked at for signs of lower motor neuron disease, such as fasciculation and atrophy.

2. *Spinal Nerves*

A spinal nerve is a mixed nerve, which is formed from the dorsal and ventral roots that come out of the spinal cord, out of the vertebrae, through the intervertebral foramen on both the sides. All spinal nerves are part of the Peripheral Nervous System (PNS). There are 31 pairs of spinal nerves.

The spinal nerves carry information to and from different levels (segments) in the spinal cord. The nerve corresponds to a segment of the vertebral column. There are

- 8 cervical
- 12 thoracic
- 5 lumbar
- 5 sacral
- 1 coccygeal nerve

The point at which the spinal cord ends is called the **conus medullaris**. It occurs near lumbar nerves L1 and L2. After

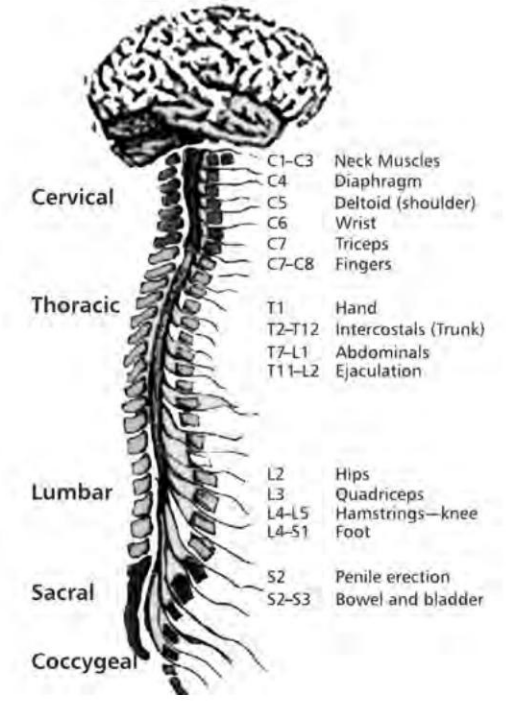


Fig. 10.4 *Spinal nerves (Refer colour figure)*

the spinal cord terminates, the spinal nerves continue as a bundle of nerves called the **cauda equine**, which resembles a horse's tail and hence the name. The upper end of the conus medullaris is usually not well defined. The lumbar, sacral and coccygeal nerves leave the vertebral canal at the appropriate lumbar, sacral and coccygeal level.

In the cervical region of the spinal cord, the spinal nerves exit above the vertebrae. A change occurs with the C7 vertebra, where the C8 spinal nerve exits the vertebra below the C7 vertebra. Therefore, there is an 8th cervical spinal nerve even though there is no 8th cervical vertebra. From the 1st thoracic vertebra downwards, all spinal nerves exit below their equivalent numbered vertebrae.

Each nerve is a mixed nerve consisting of motor and sensory components.

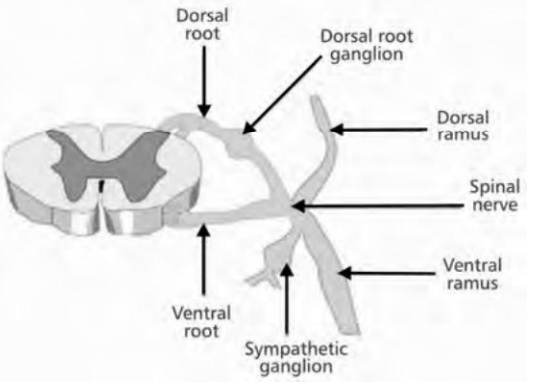


Fig. 10.5 *Formation of spinal nerve*

Each nerve also has preganglionic fibers from the sympathetic part of the autonomic nervous system.

The anterior or ventral roots carry efferent motor axons of the nerve cells in the anterior horn.

The posterior or dorsal roots carry afferent sensory axons. A small ganglion—posterior root ganglion—containing the cell bodies of sensory fibers, lies on each posterior root in the intervertebral foramina.

After passing through the foramina, the spinal nerve branches into two divisions, the anterior and posterior primary rami.

The posterior rami contains nerves that supply the posterior part of the skin and the paraspinal muscles from the head to the pelvis and carry visceral motor, somatic motor, and sensory information from these structures.

The anterior rami of thoracic spinal nerves become 12 pairs of intercostal nerves. In the other regions, they contain nerves that serve the rest of the ventral portion of the trunk and upper and lower limbs. They carry the visceral motor, somatic motor and sensory information to and back from the structures in the body wall, ventrolateral body surface and the limbs. They join together to form plexuses. A **plexus** is an interconnection of fibers. There are five voluntary plexuses. They are the cervical plexus, the brachial plexus, the lumbar plexus, the sacral plexus and the coccygeal plexus. Each plexus gives rise to new combinations of fibers as the peripheral nerves.

(a) Cervical Plexus The cervical plexus is formed by the ventral rami of the first four cervical spinal nerves which are located from C1 to C4 cervical segments in the neck. It is placed lateral to the transverse processes between prevertebral muscles. It is located in the neck, deep towards the sternocleidomastoid muscle. The nerves supply the structures at the back of the head, and some neck muscles.

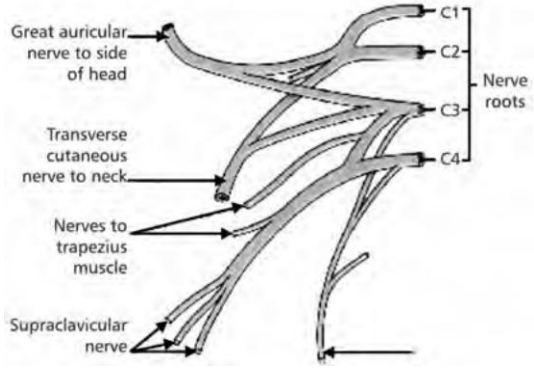


Fig. 10.6 *Cervical plexus*

The cervical plexus has two types of branches, cutaneous and muscular.

Muscular branches supply muscles of the neck—sternomastoid, trapezius, geniohyoid, thyrohyoid, sternothyroid, sternohyoid, omohyoid.

The phrenic nerve is formed from 3, 4, 5 cervical roots. It passes through the thoracic cavity to supply the pleura, diaphragm and many important structures.

(b) Brachial Plexus The brachial plexus consists of nerve fibers, formed by the ventral rami of the lower four cervical and a large part of first thoracic nerve root, specifically from above the fifth cervical vertebra to underneath the first thoracic vertebra (C5-T1). It passes through the neck and lies above and behind the subclavian vessels, enters the axilla and into the upper arm.

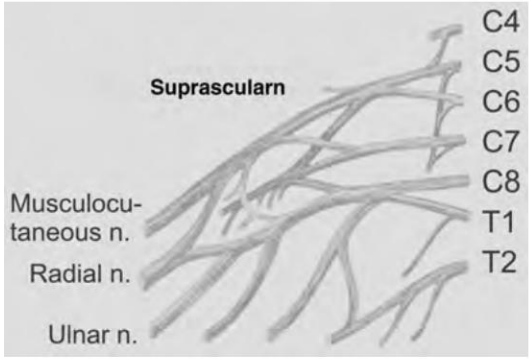


Fig. 10.7 *Brachial plexus*

Topographic divisions of the brachial plexus include the root, trunk, division, cord and peripheral nerves.

Roots combine to form **trunks.** The upper trunk is formed by the C5 and C6 roots. The C7 root continues as the middle trunk. C8 and T1 roots combine to form the lower trunk.

Each of these trunks divides into anterior and posterior divisions

The **anterior division** of upper and middle trunks forms the lateral cord. It gives rise to musculocutaneous nerve and outer branch of the median nerve.

The anterior division of lower trunk forms the medial cord and gives off the ulnar nerve, inner branch of median nerve and various cutaneous nerves.

The **posterior division** of all the trunks forms the posterior cord which gives off the axillary nerve in the axilla and continues as the radial nerve.

These **cords** are formed just above the clavicle, at the level of the first rib.

The nerves formed are the following:

Suprascapular nerve supplies supraspinatus and infraspinatus muscles.

Axillary nerve innervates the deltoid muscle, shoulder joint and the skin over the shoulder.

Musculocutaneous nerve innervates anterior skin of upper arm and elbow flexors.

Radial nerve is the largest branch. It innervates the extensors of the elbow, wrist, fingers, and abductors of the thumb. It supplies the skin on the dorsal aspect of the thumb, the first two fingers and the lateral side of the third finger.

Median nerve innervates the wrist and finger flexors. It supplies the skin of the front of the thumb, the first two fingers and the lateral half of the third finger. It helps in adduction and opponens of the thumb.

Ulnar nerve innervates the wrist and finger flexors. It also supplies the adductors and abductors of the fingers. It supplies the skin of the little finger and medial half of the third finger.

(c) Lumbar Plexus The lumbar plexus lies in the lumbar region and is part of the lumbosacral plexus. It is formed by the ventral divisions of the first three and part of the fourth lumbar nerves (L_1–L_4). The nerves pass in front of the transverse processes of the lumbar vertebrae and then go in front of the hip joint lying behind the psoas muscle. It leaves the pelvis under the inguinal ligament. The main branches of this plexus are the following:

- **Iliohypogastric nerve** supplies the muscles of the abdomen, especially transverses and internal oblique and the skin above the inguinal ligament and lateral hip.

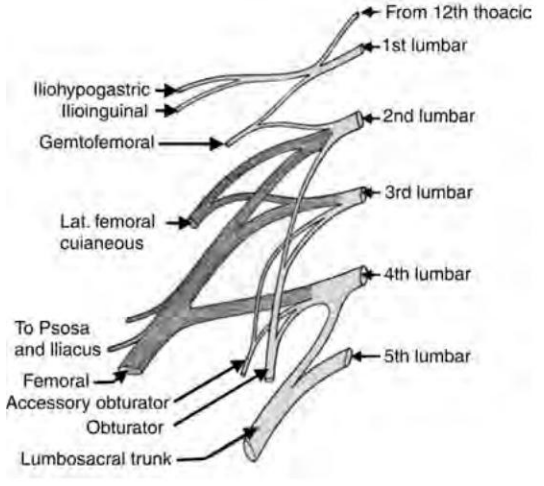


Fig. 10.8 *Lumbar plexus*

- **Ilioinguinal nerve** supplies both transverses abdominis and the skin over upper and medial part of the thigh, root of penis and lateral aspect of labia majora.
- **Genitofemoral nerve** supplies the skin over the femoral triangle and the skin of upper and inner aspects of the thigh and inguinal region. In males, it supplies the cremaster muscle.
- **Lateral cutaneous nerve of thigh** is the 1st sensory branch of lumbar plexus. It has 2 branches:

  Anterior branch supplies the skin over lateral and anterior surface of the thigh.

  Posterior branch supplies the lateral and posterior portion of the thigh.
- **Femoral nerve** is the largest and longest nerve of this plexus. In the pelvis, it runs between psoas major and iliopsoas, supplying both the muscles. It exits from the pelvis by passing behind the inguinal ligament and divides into sensory and muscular branches. The saphenous nerve supplies the medial aspect of the leg, ankle and foot. The sensory branches supply the skin in the front of the thigh, and the muscular branches supply the muscles on the anterior aspect of the thigh.
- **Obturator nerve** divides into 2 branches, anterior and posterior.

Anterior branch supplies adductor longus, and brevis and gracilis muscles.

Posterior branch supplies obturator externus and part of adductor magnus.

Sensory fibers supply the skin of the upper thigh and anastomose with the saphenous nerve.

(d) Sacral Plexus The sacral plexus is part of the lumbosacral plexus. It comes out of the sacral vertebrae. It is formed by the anterior rami of the lumbosacral trunk, the anterior division of the first sacral nerve and part of the second and third sacral nerves. The lumbosacral trunk consists of a part of the fourth lumbar and the fifth lumbar nerves.

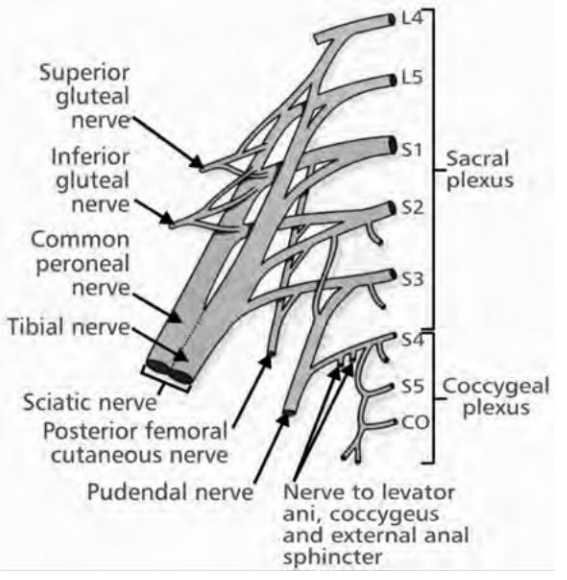


Fig. 10.9 *Sacral and coccygeal plexuses*

The nerves converge and reach the lower part of the greater sciatic foramen. Many branches arise from the band formed at this level, which supplies the pelvic organs, muscles and skin of the pelvic floor and muscles around the hip joint.

The plexus has the following branches—sciatic nerve with its branches and the pudendal nerve.

The **sciatic nerve** is the largest, longest and widest nerve in the body. It starts in the lower back, passes through the greater sciatic foramen and runs through the buttock and down the lower limb. It supplies the hamstring muscles—biceps femoris, semitendinosus and semimembranosus on the posterior aspect of the thigh.

The nerve gives off articular and muscular branches. The muscular branch gives off the tibial nerve and common peroneal nerve near the middle of the thigh.

The **tibial nerve** descends through the popliteal fossa and passes below the arch of the soleus. It supplies the gastronemius, soleus, popliteus, flexor digitorum longus, flexor hallucis longus and plantaris muscles and the skin on the posterior aspect of the leg. It continues downwards towards the feet by passing under the malleolus and supplies the muscles and skin of the heel and sole of the foot and toes.

It also gives an articular branch to the knee joint and a cutaneous branch, the sural nerve.

The **common peroneal nerve** descends along the lateral aspect of popliteal fossa, winds round the neck of the fibula close to the medial margin of biceps femoris muscle and descends into the front of the leg. It lies between the peroneus longus muscle and the fibula. It divides into superficial peroneal and deep peroneal nerves.

The superficial branch supplies the peroneus longus and peroneus brevis muscles, the skin on the lateral aspect of the leg and ankle and a part of the dorsum of the foot.

The deep branch supplies the muscles of the anterior compartment—tibialis anterior, extensor digitorum longus and brevis extensor hallucis longus and peroneus tertius.

The **sural nerve** originates from the union of medial sural cutaneous branch of tibial nerve and sural communicating branch of common peroneal. It supplies the area of heel, lateral aspect of ankle and a part of the dorsum of foot.

The **pudendal nerve** is a somatic nerve. It supplies the external genitalia, the sphincters of the bladder and the rectum.

3. Brain

The brain constitutes 1/50th of the body weight. It weighs about 1.5 kg. It is protected by a bony cage called the skull or the cranial cavity. Two cerebral hemispheres form the largest part of the brain and are attached to the brain stem. The cerebellum lies beneath the cerebrum and behind the brain stem.

All the parts of the brain work together, but each part has its own special functions. The brain can be divided into three basic units:

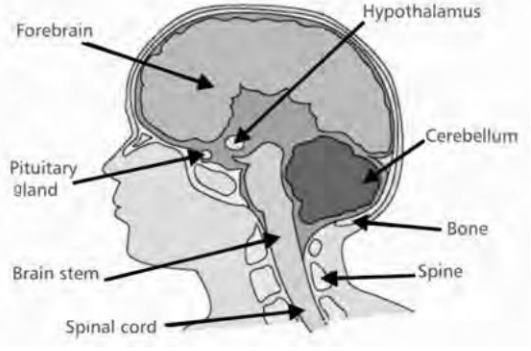


Fig. 10.10 *Parts of the brain*

- Forebrain
- Midbrain
- Hindbrain

The **forebrain** is the largest and most highly developed part of the human brain. It consists of the cerebrum, basal ganglia, limbic system, reticular formation, thalamus and hypothalamus.

The **midbrain** lies between the forebrain and the hindbrain. It consists of the brain stem, and as a major part of the extrapyramidal system—red nucleus, substantia nigra, tectum, tegmentum and corpus striatum.

The **hindbrain** includes the brain stem and the cerebellum. It controls the body's vital functions and processes such as respiration and heart rate. The cerebellum coordinates these movements.

(a) Cerebrum The cerebrum is the largest part of the brain. It is located in the anterior portion of the skull and is divided into two hemispheres by a deep groove, called the **longitudinal cerebral fissure**, and has a fold of dura mater called the **falx cerebri**. It penetrates into the depth of the brain and reaches up to the corpus callosum which is a mass of white matter consisting of nerve fibers connecting both the hemispheres.

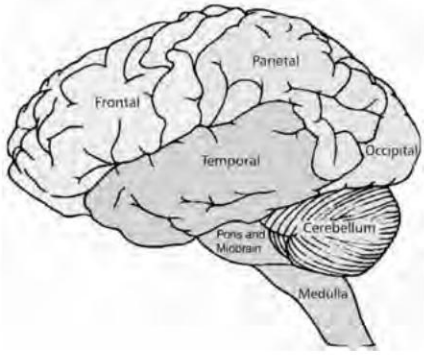


Fig. 10.11 *Cerebral cortex*

In the cerebrum, there are 100 billion neurons. The different parts of the cerebrum carry out various functions for the opposite side of the body. The right side of the cerebrum controls things such as imagination and 3D forms. The left side controls numbering skills, posture, and reasoning.

The hemispheres consist of an inner core, called the **white matter** which consists of nerve fibers, and the cortex (the superficial part of the cerebrum), the wrinkly, outer grey layer, which contains the neurons. It is called the **gray matter**.

Each hemisphere is divided into four lobes and they are separated by sulci which are called fissures.

The **lobes** are frontal, parietal, temporal, and occipital lobes. Each lobe controls a different range of activities.

Sulci are the central sulci, the lateral sulci and the parieto-occipital sulci.

The afferent and efferent fibers link the different parts of the brain. These fibers are named according to the functions they perform.

(1) **Association fibers** connect different parts of the cerebral hemisphere by extending from one gyrus to another.
(2) **Commissural fibers** connect corresponding areas of the two cerebral hemispheres, the largest of these being the corpus callosum.
(3) **Projection fibers** connect the cerebral cortex to lower parts of the brain and spinal cord, e.g., internal capsule.

Functions of the Brain

1. The brain is concerned with all **higher mental functions**, such as thinking and memory.
2. It also controls the movements of the body and functions like speech, hearing, vision, smell, perception of **sensations** like pain, touch, temperature, etc.
3. It determines intelligence, personality, interprets sensory impulses, is concerned with planning and organization and governs all conditional reflexes.
4. The cerebrum is responsible for initiation and control of **voluntary movements** of the body, carried out by skeletal muscles. It carries out special motor functions, like regulation of tone, equilibrium and posture, through the autonomic nervous system.
5. Within Broca's area, thoughts are translated into **speech**, and muscles are coordinated for speaking. Impulses from other motor areas direct our hand muscles, when we write and our eye muscles, when we scan a page for information.
6. The surface of the cerebrum is formed by sulci and gyri. The central sulcus divides the cortex into precentral gyrus (the motor cortex) and postcentral (sensory cortex) gyrus.

Motor Areas The motor cortex is involved in the planning, controlling and executing the voluntary motor functions. It can be divided into

- The primary motor cortex, or the precentral area
- The secondary motor cortex

Primary Motor Cortex It lies in the posterior portion of the frontal lobe, anterior to the central sulcus. It is responsible for generating the neural impulses, controlling execution of movement and works in association with the premotor areas. It is responsible for initiation and execution of contraction of skeletal muscles.

The nerve cells in the motor cortex are called **Betz cells** and are pyramidal in shape. These cells give rise to fibers which form the pyramidal tract. The fibers cross to the opposite side in the medulla oblongata. Hence, motor area of one (right) hemisphere controls voluntary muscle movements of the other (left) side of the body.

In motor area, the body is represented upside down. The cells nearest the vertex control the muscles of the feet and those in the lower part control the muscles of the head, neck, face and fingers.

Secondary Motor Cortex—The **posterior parietal cortex** lies behind the post-central area. It is responsible for transforming visual information into motor commands. It helps in obtaining and retaining accurate knowledge of objects. Objects can be recognized by touch alone because of knowledge from memory retained in this area.

The **premotor cortex** lies in the frontal lobe, anterior to the motor area. It guides eye and head movements and a person's sense of orientation. It probably influences the motor area.

Above the lateral sulcus is the **Broca's area,** which is the speech area and controls movements of muscles for speech. In right-handed people, it is located in the dominant left hemisphere.

The **supplementary motor area** is responsible for planning and coordinating complex movements such as those requiring the use of two hands.

The **Frontal area** is highly developed in humans. Communication occurs between this area and other areas of the brain. The frontal lobe or prefrontal association complex is involved in planning actions and movement, as well as abstract thoughts.

Association areas are localized in the parietal-temporal-occipital complex, typically in the left hemisphere.

Association areas are concerned with emotions and intellectual processes, by connecting sensory and motor functions. In association areas, innumerable impulses are processed that result in memory, emotions, judgment, personality and intelligence.

Sensory Areas The **sensory area** lies behind the central sulcus in the post-central area. It receives and processes sensory information from various parts of the body. Parts of the cortex that receive sensory inputs from the thalamus are called primary sensory areas. The primary visual cortex is responsible for vision; primary auditory cortex, for hearing; and primary somatosensory cortex, for touch. Each hemisphere receives information from the opposite side of the body.

The **sensory speech area** lies in the lower part of the parietal lobe and extends into the temporal lobe. Spoken words are perceived here. This area is in the left hemisphere in right-handed persons.

The **olfactory area** lies deep in the temporal lobe. Impulses from the nose, via the olfactory nerves, are received and perceived.

The **taste area** lies above the lateral sulcus. Impulses from special nerve endings in the taste buds of the tongue and lining of cheeks, palate and pharynx come here and thus taste is perceived.

(b) Internal Capsule The internal capsule is an important area consisting of projection fibers. It lies deep in the brain. Many impulses pass to and from the cerebral cortex to other parts of the nervous system and are carried by fibers that form the internal capsule. Motor fibers, within the internal capsule, form the pyramidal tracts that decussate in the medulla oblongata.

(c) Other areas of the Cerebrum There are a collection of nuclei deep inside the white matter of the cerebral cortex. They act as relay stations and impulses are passed from one neuron to another. They are

- Basal ganglia
- Thalamus
- Hypothalamus

(i) Basal Ganglia The basal ganglia are a collection of nuclei found on both sides of the thalamus, outside and above the limbic system, but below the cingulate gyrus and within the temporal lobes. Basal ganglia are a part of the extrapyramidal system. Glutamate is the most common neurotransmitter. The inhibitory neurotransmitter GABA also plays an important role in the functioning of the basal ganglia.

This is discussed in detail in the extrapyramidal system.

(ii) Thalamus The two thalami are located in the center of the brain, one beneath each cerebral hemisphere, on either side of the third ventricle below the corpus callosum in the posterior part of the forebrain.

Above each thalamus is the lateral ventricle. They are joined by a bridge of gray matter, the **massa intermedia**, stretching across the third ventricle. Below and in front of each thalamus is the hypothalamus, and to its side is the internal capsule.

The thalamus splits into three major parts, viz., lateral, medial and anterior, by a thin, Y-shaped fibrous sheet.

It serves as a relay station for nerve impulses carrying sensory information to the brain. Sensory impulses come here from the skin, viscera and special senses. It receives these sensory inputs as well as inputs from other parts of the brain and determines which of these signals are to be forwarded to the cerebral cortex. It also receives input from the cerebellum, basal ganglia, limbic system and reticular formation. Impulses of pain, touch, temperature and kinesthetic sensations are relayed here.

(iii) Hypothalamus The hypothalamus is a portion of the brain that contains a number of small nuclei with a variety of functions. It is located below the thalamus, just above the pituitary gland in the middle of the base of the brain and encapsulates the ventral portion of the third ventricle.

One of the most important functions of the hypothalamus is to link the nervous system to the endocrine system via the pituitary gland. It is connected with the anterior lobe of the pituitary gland through blood vessels and with the posterior lobe through nerves.

It is connected with the midbrain, the brain stem reticular formation, basal nuclei and certain other regions of the cerebral cortex.

Functions

1. It is responsible for certain metabolic processes and other activities of the autonomic nervous system. It synthesizes and secretes neurohormones, often called hypothalamic-releasing hormones and these, in turn, stimulate or inhibit the secretion of pituitary hormones, both from anterior and posterior pituitary.
2. The hypothalamus controls body temperature by its autonomic effects like respiration and circulation.
3. It controls hunger, thirst, appetite, feeding and obesity.
4. It has a control on the circadian rhythm. Circadian rhythm is for sleeping, waking and diurnal variation of body temperature.
5. It controls gastric secretion and emotional behaviors like anger and pleasure.
6. The hypothalamus is also responsible for sexual behavior.

4. Brain Stem

The brain stem is the lower extension of the brain, adjoining and structurally continuous with the spinal cord. The cranial nerves (with the exception of 1 and 2) originate in the brain stem. All efferent and afferent pathways, between the cerebrum and cerebellum, course through the brain stem and many of them decussate or cross here. It also has nuclei important for sympathetic and parasympathetic autonomic functions. Its neurological functions include those necessary for survival (breathing, digestion, heart rate, blood pressure) and for arousal (being awake and alert).

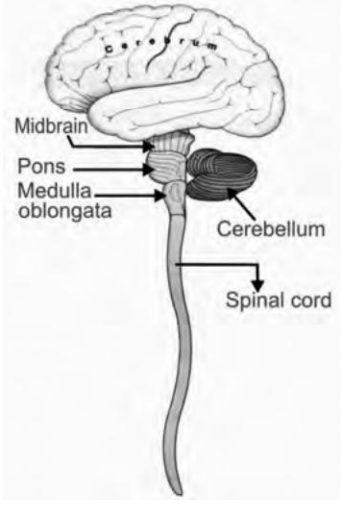


Fig. 10.12 *Parts of the central nervous system*

The brain stem is located in an area near bony protrusions, making it vulnerable to damage during trauma. Important

neural structures lie here and hence even very small lesions of the brain stem may have profound effects.

The brain stem consists of the midbrain, pons and medulla. Reticular formation is also included by some.

(a) Midbrain The midbrain is the smallest region of the brain. It is situated around the aqueduct between the cerebrum above and pons below. It is a connecting link between the forebrain and hindbrain.

The midbrain consists of groups of cell bodies and nerve fibers. It has pathways connecting the cerebrum with the lower parts of the brain and the spinal cord. It consists of the red nucleus, crus-cerebri, substantia nigra, tegmentum and tectum. The red nucleus and the substantia nigra are involved in the control of body movements.

It is, thus, the center for righting and postural reflexes mediated through visual and auditory impulses.

(b) Pons Pons is located superior to the medulla oblongata, caudal to the midbrain, and ventral to the cerebellum.

There are groups of cells in the pons which act as relay stations but it mainly consists of nerve fibers which forms a bridge between the two hemispheres of the cerebellum and also connects higher structures to the spinal cord.

The anatomy of the pons differs from the anatomy of the cerebrum. The nerve fibers lie on the surface while the cell bodies lie deep in the substance of pons.

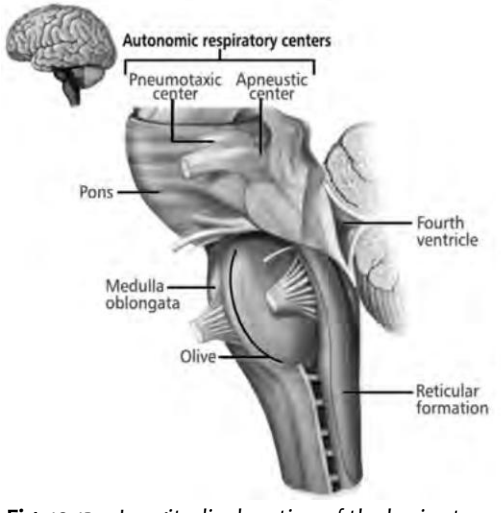


Fig. 10.13 *Longitudinal section of the brain stem*

Functions It controls sexual arousal and regulates respiration. It is responsible for sleep and dreaming, and relays sensory information between the cerebrum and the cerebellum.

(c) Medulla Oblongata The medulla oblongata is the lower portion of the brain stem. It lies below the pons, is continuous with the spinal cord below and is within the cranium above the foramen magnum. It is 2.5 cm long. Anterior and posterior surfaces of the medulla oblongata are marked by fissures.

Gray matter lies centrally and white matter is on the outer side. Motor nerves coming from the cerebrum cross in the medulla to the opposite side. They are the main pathway for impulses to skeletal muscles. So, due to this crossing, the left hemisphere of the cerebrum controls the right half of the body and vice versa. Some sensory nerve fibers ascending to the cerebrum cross in the medulla.

Functions and Properties

1. It deals with autonomic functions. It relays signals between the brain and spinal cord.

   The respiratory centre controls rate and depth of respiration. Increase in pCO_2 and decrease in pO_2 stimulate the respiratory center. Chemoreceptors also stimulate the respiratory center. So nerve impulses from the respiratory center pass to phrenic and intercostals nerves, which stimulate contraction of diaphragm and intercostal muscles respectively.
2. The vasomotor center controls the diameter of small arteries and arterioles. Impulses from the vasomotor center pass to the blood vessels through the autonomic nervous system and cause vasodilatation or vasoconstriction.
3. Impulses from baroreceptors or any change in the body temperature or emotional changes send impulses to the vasomotor center and stimulate the center.
4. Pain causes vasoconstriction, but severe pain causes vasodilatation, decrease in blood pressure and even fainting.
5. The cardiac center is the part of the medulla oblongata responsible for controlling the heart rate and force of contraction of the heart. Both sympathetic and parasympathetic fibers go to the heart. Sympathetic stimulation increases heart rate and stroke volume of the heart, while parasympathetic stimulation decreases heart rate and force of contraction.
6. The medullary functions are associated with the nuclei of the glossopharyngeal, vagal, spinal accessory, and hypoglossal nerves. The medulla controls the reflex actions of the pharynx, larynx, and tongue, which are related to deglutition, speech and mastication, as well as the visceral reflexes of coughing, sneezing, sucking, vomiting, salivating and other secretory functions. Irritation from stomach, pharynx or larynx sends impulses to the medulla oblongata and stimulates the reflex centers which initiate reflex actions of coughing, sneezing or vomiting to expel the irritant.

(d) Reticular Activating System The reticular activating system, or reticular formation, is a set of diffuse and poorly differentiated collection of neurons located in the core of the brain stem. Its dorsal tegmental nuclei are in the midbrain, while its central tegmental nuclei are in the pons, and its central and inferior nuclei are found in the medulla. Due to many

synaptic links with other parts of the brain, it is an important information centre. The ascending reticular activating system connects to the cortex, thalamus and hypothalamus. The descending reticular activating system connects to the cerebellum and sensory nerves.

The **ascending reticular activating system** is responsible for the sleep–wake cycle due to its connection with the thalamus, which plays a role in wakefulness (information is sent to the cortex) thus, mediating various levels of alertness. Due to this property, it selectively blocks or passes sensory information, as much as is necessary, e.g., a mother immediately gets up when her sick child makes the slightest sound, while other loud noises like the sound of a train may not be heard in sleep.

Visual and auditory impulses are relayed here.

The **descending reticular formation** is involved in coordination of skeletal muscle activity, voluntary motor movements and thus, maintenance of posture and equilibrium. It helps in coordination of various activities and does this with the help of the autonomic nervous system, e.g., respiratory, cardiovascular and gastro-intestinal activity. It receives information from the hypothalamus and is also involved in reflexive behavior, such as coughing, chewing, swallowing and vomiting.

Anesthetics and hypnotics have their effects by acting on the reticular formation.

The reticular formation also receives some of the cortico-bulbar fibers from the motor cortex. It innervates the three cranial nerves involved in eye movement. Other cortico-bulbar fibers innervate cranial nerves directly.

5. Limbic System

The limbic system is a set of structures which includes the thalamus, hippocampus, amygdala, hypothalamus, septum, limbic cortex and a part of the reticular formation. It operates by influencing the endocrine system and autonomic system. It is concerned with emotions like love, hate, revenge, envy, long-term memory, motivation and olfaction. It acts as a form of emotional homeostasis and also plays a role in sexual arousal. It is also involved in feelings of getting pleasure on solving problems.

The amygdala and hippocampus play important roles in memory and for determining what memories are stored and where they are stored in the brain.

6. Cerebellum

The cerebellum is the largest part of the hind brain. It is situated in the posterior fossa just above the brain stem, behind the pons and medulla. On the notch anteriorly rest the pons and the medulla.

It has two hemispheres connected to each other through a median structure called the **vermis**. It contains gray matter on the surface and white matter deeply.

Within the white matter, there are four deep cerebellar nuclei, which act as the main centers of communication.

The cerebellum has two surfaces—superior and inferior. The inferior surface has a deep median notch which separates the right and left hemispheres.

Each hemisphere is divided into three lobes—anterior, middle, and flocculonodular lobe.

- The **anterior lobe** lies on the anterior part of the superior surface.
- The **middle lobe** is the largest of the three lobes and is separated from the anterior lobe by fissure prima and posterolateral fissure.
- The **flocculonodular lobe** is the smallest lobe and lies on the inferior surface.

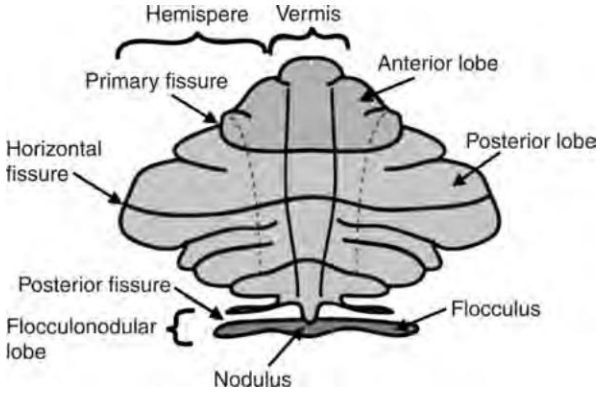


Fig. 10.14 *Cerebellum*

The cerebellum is further subdivided into numerous small parts by fissures, and each fissure cuts into the vermis and both hemispheres.

Fibers entering or leaving the cerebellum are grouped to form three peduncles which connect the cerebellum to the midbrain, pons and medulla.

The superior cerebellar peduncle is chiefly efferent, while middle and inferior peduncles are chiefly afferent.

Functionally, it is divided into three parts:

- The **archicerebellum** is the oldest part and consists of flocculonodular lobe and lingual lobe. It is connected to the vestibular part of the ear. It controls locomotion and maintains equilibrium.
- The **paleocerebellum** is the next part to appear during development and evolution and consists of anterior lobe, pyramid and uvula. It is chiefly spinocerebellar in connection and controls tone, posture and crude movements of limbs.
- The **neocerebellum** is the newest part of the cerebellum. It consists of middle lobe minus pyramid and uvula. It is chiefly cortico-cerebellar in connection and its main function is regulation of fine movements of the body.

(a) Functions

1. The cerebellum plays an important role in the integration of sensory perception, coordination of voluntary motor

movements, balance, posture, equilibrium and muscle tone. It gets input from other areas of the brain, spinal cord and sensory receptors, to provide precise timing for coordinated, smooth movements of the skeletal muscular system. It controls the same side of the body. It is especially active during rapid motor activity.

Most of the movements are pendular. It helps to stop movement at the intended point by sending necessary signals and thus, prevents overshooting.

2. Information from periphery is detected and the cerebellum predicts the movements, and agonists are inhibited and antagonists are excited.
3. It predicts the distance a limb has to move (traverse) to reach the target. Progression of one movement to another occurs in a sequential fashion.
4. It regulates eye movements. Certain movements while reading, looking from the window while traveling in a car or train are ballistic movements and for this, the cerebellum is essential.
5. Proprioceptors from muscles and joints indicate their relation to the body and along with impulses from the eyes and ears; information is available regarding the position of the head in space.

(b) Disorders The cerebellar dysfunction is characterized by impairment of gait (ataxia), incoordination (dysmetria), disordered eye movements, poor articulation in speech (dysarthria), impaired swallowing (dysphagia) and tremor.

Balance is poor, walking is characterized by a widened base and turning is difficult and can result in falls. The person walks in a zigzag manner and deviates to one side, i.e., the same side as the lesion.

There is dysmetria of the extremities leading to dysdiadochokinesis (the impairment of alternating movements, e.g., rapid pronation and supination movements), dysrhythmic tapping of feet or hands.

There is decomposition of movement and when the part in action reaches near the target, there are jerky movements.

Tone is decreased, leading to hypotonia.

Rebound phenomenon occurs (overcorrection of passive displacement) of the limb and there is overshooting of the affected extremity. Tremors of extremities, head and trunk (titubation) are seen.

Speech is characterized by scanning dysarthria with alteration in rate (slower), rhythm (irregular), and force (variable volume). There is slurring of speech and tremor of the voice. Resultant speech is unintelligent.

Nystagmus is present with horizontal and less often, with vertical gaze.

7. Extrapyramidal System (EPS)

The extrapyramidal system is that part of the nervous system which regulates muscle reflexes and reflex movements such as balance and walking. It consists of nerve cells, tracts that connect the cerebral cortex, basal ganglia, thalamus, cerebellum, reticular formation and spinal neurons.

Basal Ganglia Basal ganglia are a collection of nuclei found on both sides of the thalamus, outside and above the limbic system, below the cingulate gyrus and within the temporal lobes.

It includes the corpus striatum, subthalamic nucleus, substantia nigra, and red nucleus along with their interconnections with the reticular formation, cerebellum and cerebrum. The largest group is the corpus striatum, which consists of the caudate nucleus, the putamen, the globus pallidus and the subthalamic nucleus.

GABA, the inhibitory neurotransmitter, plays the most important role in the basal ganglia. It regulates muscle reflexes, locomotion, complex movements for postural control. It regulates reflex movements such as balance and walking. It modulates motor activity without directly innervating motor neurons.

From each side of the motor cortex and premotor area, fibers are projected into the caudate nucleus and putamen. From here, fibers are projected to globus pallidus and substantia nigra. Fibers from caudate nucleus to substantia nigra are excitatory. They secrete the inhibitory neurotransmitter dopamine whose main function is to inhibit the release of prolactin from the anterior lobe of the pituitary.

From globus pallidus group of fibers called **Ansa lenticularis**, reach the venteroantral and ventrolateral nucleus of thalamus and subthalamic nucleus, viz., substantia nigra and red nucleus. The same thalamic nucleus receives signals from the cerebellum. These fibers are projected to the motor cortex and premotor cortex. Fibers from the thalamic nucleus end in the caudate nucleus and putamen and secrete acetylcholine.

The red nucleus receives signals from the basal ganglia, cerebral cortex and cerebellum and they are projected to reticular formation and spinal cord.

The brain-stem nucleus also projects to caudate nucleus which secretes the inhibitory neurotransmitter, serotonin. This pathway is important for inducing sleep.

The main function of substantia nigra is controlling eye movements. It also controls muscle tone.

Voluntary activities initiated by the cerebral cortex are controlled by basal ganglia.

Automated associated movements, viz., swinging movements of the hands while walking, are controlled by it.

Due to its connection with reticular formation, it is also involved in sexual arousal mechanism.

The basal ganglia functions in association with cerebral cortex for both motor control and sensory activities.

8. Meninges

The meninges are membranes which cover the brain and spinal cord. It consists of three layers: the dura mater, the arachnoid mater and the pia mater. The primary function of the meninges and of the cerebrospinal fluid is to protect the central nervous system.

(a) Dura Mater The dura mater is a thick, durable membrane, closest to the skull and is the most resilient of the three. It consists of two layers, the periosteal layer is the superficial layer which serves as the skull's inner periosteum and is called the **endocranium**. The deeper layer is the actual dura mater. It is composed of dense fibrous tissue and its inner surface is covered by flattened cells.

The dura mater envelops the arachnoid and between these two is a potential space called the subdural space. It surrounds and supports the large venous channels or cranial sinuses (dural sinuses). The sinuses drain blood and cerebrospinal fluid from the brain and into the internal jugular vein and finally into the heart.

(a) Arachnoid Mater The middle layer of the meninges is the arachnoid membrane which is delicate, thin, transparent and fibrous. It provides a cushioning effect for the central nervous system. It is composed of fibrous tissue and is covered by flat cells and is impermeable to fluid. A large number of fine filaments called **arachnoid trabeculae** pass from the arachnoid and blend with the tissue of the pia mater. This subarachnoid space contains cerebrospinal fluid. The arachnoid and pia mater are together called **leptomeninx** or **leptomeninges**.

(c) Pia Mater The pia mater is a very thin, delicate membrane. It is the meningeal envelope which firmly adheres to the surface of the brain and spinal cord. It follows all the minor contours of the brain (gyri and sulci). It is covered, on its outer surface, by a sheet of flat cells and is impermeable to fluid. It is adherent to the brain by the processes of astrocytes. It is pierced by blood vessels, which enter the brain and spinal cord and its capillaries provide nourishment to the brain. Along with the ependyma lining the ventricles, it forms choroid plexuses which produce the cerebrospinal fluid.

9. Cerebrospinal Fluid

Cerebrospinal Fluid (CSF) is a clear, colorless, watery fluid that occupies the subarachnoid space, the ventricular system and the central canal of the spinal cord.

It is produced by the cells of the choroid plexus (70%) and the remainder is formed by blood vessels and secreted by ventricular walls. It circulates from the choroid plexus through the foramen of Monro into the third ventricle, and then through the cerebral aqueduct into the fourth ventricle. It, then, flows through the cerebellomedullary cistern down the spinal cord and over the cerebral hemispheres. CSF, then, passes back into the blood through the arachnoid villi. The movement of CSF takes place depending on the pressure difference. When CSF pressure is higher than venous pressure, CSF passes into the venous sinuses; and when venous pressure is higher, blood constituents do not pass into CSF.

CSF contains water, glucose (40 to 60%), electrolytes like sodium, potassium, calcium, chloride and small amounts of albumin, globulin, urea and creatinine.

Functions

1. It supports and protects the brain from damage by buffering action. It acts like a cushion.
2. The brain is immersed in fluid; hence, the net weight of the brain is reduced from about 1,400 g to about 50 g. Therefore, pressure at the base of the brain is reduced. This is called buoyancy.
3. It is the medium for supplying nutrition to the brain and spinal cord and takes away the waste products.
4. CSF serves to transport hormones to other areas of the brain. Hormones released into the CSF can be carried to remote sites of the brain, where they may act.

It is of great diagnostic importance. By carrying out lumbar puncture, CSF examination is helpful in diagnosing meningitis (infective and tubercular) and hemorrhage.

10. Ventricles of the Brain

The brain ventricular system consists of four communicating cavities that are continuous with the central canal of the spinal cord and contain cerebrospinal fluid.

The four ventricles are the two lateral ventricles, the third ventricle and the fourth ventricle.

The **two lateral ventricles** are located within the cerebrum, are relatively large and C-shaped, on either side of the median plane. They communicate via the interventricular foramina with the third ventricle. They are separated by a thin membrane called **septum lucidum**.

The **third ventricle** communicates with the fourth ventricle via the aqueduct, which is located in the midbrain. It lies between the two parts of the thalamus.

The three foramina to the subarachnoid space are found in the **fourth ventricle**. This permits cerebrospinal fluid, produced in the ventricles, to surround the brain stem, cerebellum and cerebral cortex. The fourth ventricle is continuous with the central canal of the spinal cord, allowing the CSF to bathe the inside surface of the spinal cord.

These ventricles allow the CSF to flow through them, which is necessary for protection of the brain and for removal of metabolites.

11. Blood–Brain Barrier

The Blood–Brain Barrier (BBB) is a cellular structure in the Central Nervous System (CNS), allowing the passage of

substances, essential to metabolic function (e.g., oxygen), and restricts the passage of certain substances and microscopic objects (e.g., bacteria), between the bloodstream and the neural tissue.

This restriction of passage of substances is due to high-density cells as compared to the endothelial cells in capillaries elsewhere in the body. The tight junctions and basal lamina of the cerebral endothelial cells play the most substantial role in maintaining the barrier.

Capillaries are lined with endothelial cells having small spaces between each individual cell, so substances can readily move in and out. However, in the brain, the endothelial cells fit tightly together so substances cannot pass out of the bloodstream.

(a) Properties Large molecules do not pass through the BBB easily.

Lipid (fat)-soluble molecules do not penetrate into the brain, except barbiturates, which rapidly crosses through into the brain.

Molecules that have a high electrical charge pass slowly.

Trauma, radiation, inflammation, microwaves, pressure or ischemia can injure and open the BBB and can alter its permeability.

(b) Functions

1. It protects the brain from foreign substances present in the blood that may injure the brain.
2. It protects the brain from hormones and neurotransmitters present in the rest of the body.
3. It maintains a constant environment for the brain.

12. *Spinal Cord*

(a) External Structure

The spinal cord is the lower, elongated, cylindrical part of the central nervous system, flattened antero-posteriorly. It is covered by three layers of tissue called **meninges**. The spinal cord and meninges are contained in the spinal canal. It is protected by the bony vertebral column. The vertebrae are separated by disks made of cartilage, which act as cushions, reducing the forces generated by movements such as walking and jumping.

It is 45 cm long and is as thick as the thickness of the little finger.

It is continuous above with the medulla oblongata. It extends from the upper border of the atlas or foramen magnum to the lower border of the 1st lumbar vertebra.

The lower end of the spinal cord is conical and is called the **conus medullaris**. The apex of the conus continues downwards as the filum terminale.

The cord has two thickenings—cervical and lumbar—which give rise to the nerves of the limbs.

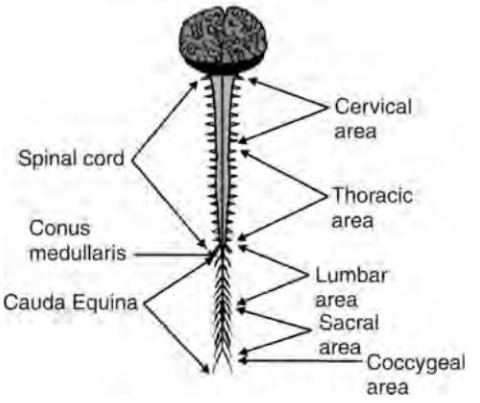


Fig. 10.15 *The spinal cord*

The spinal cord gives off 31 pairs of spinal nerves. Spinal nerves consist of nerve fibers that carry incoming and outgoing messages between the brain and the rest of the body. It is the center for reflexes called spinal reflexes. These actions are independent (without messages from the brain).

Details of spinal nerves have been discussed earlier.

(b) Internal Structure A cross section of the spinal cord shows that the central part contains gray matter, consisting of cells, which is surrounded by white matter consisting of fibers. The gray matter has a roughly H-shaped or 'butterfly' outline. It is composed of nerve cells and neuroglia. It consists of the dorsal horn, ventral horn and lateral horn.

The **gray matter** of right and left halves of the spinal cord is connected across the midline by the gray commissure, traversed by the central canal, which runs throughout the entire length of the spinal canal. The portion of gray matter in front of the canal is called the **anterior gray commissure** and that behind is called the **posterior gray commissure**.

The central canal is an extension from the 4th ventricle and contains cerebrospinal fluid.

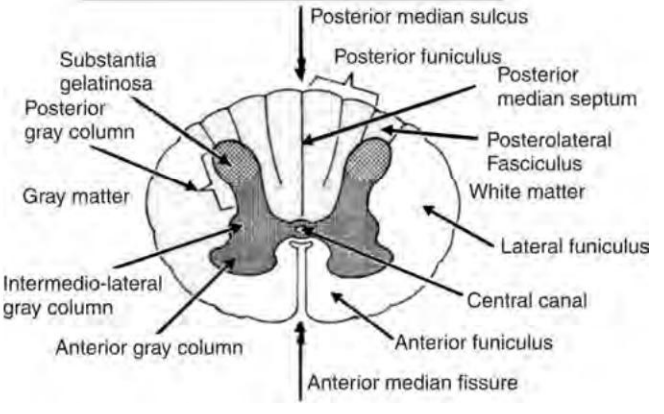


Fig. 10.16 *Transverse section of the spinal cord*

The **neurons** in the spinal cord are the following:

- **Sensory neurons** receive impulses from the periphery of the body.

- **Motor neurons** of the ventral horn supply the skeletal musculature and consist of alpha and gamma motor neurons. They transmit impulses to the skeletal muscles.
- **Connecting neurons** link sensory and motor neurons at the same level or at different levels.

The cells of the lateral horn and the sacral autonomic nucleus are preganglionic neurons of the sympathetic and parasympathetic divisions of the ANS, respectively.

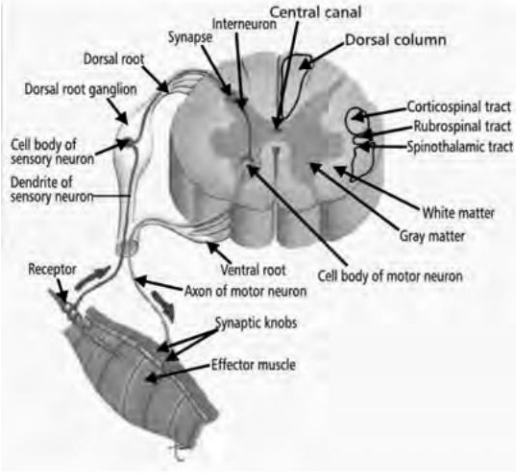


Fig. 10.17 *Cross-section of the spinal cord and the three types of neurons, spinal nerve*

There is increased volume of gray matter in the cervical and lumbosacral enlargements for innervation of the limbs.

The **anterior column of gray matter** contains cell bodies of lower motor neurons, which form nerves to supply the muscles and other effector organs.

The **posterior column of gray matter** contains the cell bodies which receive the sensory impulses from the periphery of the body. These cells give rise to nerve fibers, which form the white matter of the cord. The posterior root ganglia lie on the pathway of the sensory nerves outside the spinal cord and consist of neurons, and the sensory fibers pass through these ganglia.

The **white matter** consists of fibers. It consists of 3 funiculi or columns—dorsal (or posterior), lateral and ventral (or anterior) columns, each of which contains axon tracts related to specific functions. These columns are the sensory nerve fibers ascending to the brain; motor nerve fibers descend from the brain and there are fibers of connector neurons. These columns are also known as **tracts**. They are named according to their points of origin or destination, e.g., the spinothalamic is the tract running from the spinal cord to the thalamus.

An anterior median fissure and a posterior median sulcus incompletely divide the spinal cord into two symmetrical parts. There is a commissural band of nervous matter called the anterior white commissure which connects the two halves.

The nerves are grouped in different bundles called ascending and descending tracts.

(i) Ascending or Sensory Nerve Tracts **Ascending tracts** carry information from the body from somatic mechanoreceptors. They form the dorsal column and transmit sensations from the periphery to the brain via the spinal cord.

They are

(1) **Tracts in the posterior funiculus**
- Fasciculus gracilis (medially)
- Fasciculus cuneatus (laterally)

They are also called posterior column tracts.

(2) **Tracts in the lateral funiculus**
- Lateral spinothalamic tract
- Anterior and posterior spinocerebellar tracts
- Spino olivary tract
- Spino tectal tract

(3) **Tracts in the anterior funiculus**

(ii) Anterior Spinothalamic Tract Sensory receptors are stimulated by touch, pain, heat, cold and pressure. The nerves carry these sensations to the spinal cord from where these ascending tracts carry them to the opposite hemisphere of the cerebrum.

Decussation or crossing to the other side occurs either at the level of entry or in the medulla.

The sensory receptors in the tendons, muscles and joints are called **proprioceptors** and are stimulated by stretch. Along with impulses from eyes and ears, they help maintain posture and balance.

Some of these impulses reach the sensory area of the opposite cerebral hemisphere. Some impulses reach the cerebellar hemisphere on the same side.

(iii) Descending or Motor Nerve Tracts The descending tracts transmit impulses from the brain to the periphery and initiate movement and control body functions.

They are the following:

(1) **Corticospinal tract** descends from the cerebral cortex to spinal cord. They are also called pyramidal tracts.
It consists of 2 parts:
- *Lateral corticospinal tract* which lies in the lateral funiculus
- *Anterior corticospinal tract* which lies in the anterior funiculus

(2) **Rubrospinal tract**
(3) **Olivospinal tract**
(4) **Vestibulospinal tract**
(5) **Tectospinal tract**
(6) **Lateral and medial reticulospinal tract**
(7) **Medial longitudinal bundle**

Thus, the major descending tracts are the pyramidal and extrapyramidal tracts.

The **pyramidal tract** has its origin in the precentral gyrus from the Betz cells or pyramidal cells. 80% arise here. The remaining 20% arise from the postcentral gyrus of the parietal lobe. The axons of these cells descend down and converge at the internal capsule. They descend in the medulla, and most of the fibers cross to the opposite side in the pyramidal decussation and form the lateral white column of the spinal cord. The fibers, which do not cross, descend in the anterior white column of the spinal cord. They end in the anterior cells of the spinal cord. The lower motor neuron from here innervates the muscles of the extremities. They are the motor pathway for controlling voluntary movements of the body, especially the movements of fingers, toes and hand. They also are pathways for superficial reflexes like abdominal and planter reflexes.

10.1.3 Autonomic Nervous System

The Autonomic Nervous System (ANS) is a part of the peripheral nervous system. It acts as a control system and acts involuntarily below the level of consciousness and controls visceral functions such as digestion, regulation of respiration, secretion from glands, etc. It plays a very important role in maintaining homeostasis in the body.

It acts mainly on cardiac muscles, smooth muscles, pupils, blood vessels and glands.

It can be divided into the parasympathetic nervous system and sympathetic nervous system.

The enteric nervous system is a third division of the autonomic nervous system. It is a meshwork of nerve fibers that innervate the viscera (gastrointestinal tract, pancreas and gall bladder).

Sympathetic and parasympathetic divisions function in opposition to each other. The ANS acts through a balance of these two components. Structurally and functionally, they differ. Sympathetic activity acts in stressful conditions, while the parasympathetic system acts at rest.

1. Sympathetic Nervous System (SNS)

The preganglionic motor neurons of the sympathetic system arise in the spinal cord. They begin at the first thoracic segment and extend up to the second or third lumbar segments; hence, the SNS is also called the **thoracolumbar outflow**. They pass into sympathetic ganglia, which are organized into two chains that run parallel to and on either side of the spinal cord.

The preganglionic fibers leave the spinal cord through the anterior nerve root and synapse with the postganglionic neurons situated in the sympathetic ganglia which are of three groups—paravertebral, prevertebral and terminal. Then the postganglionic neurons go across most of the body. The sympathetic ganglia lie near the spinal cord and away from the organs they supply. These ganglia are attached to each other by nerve fibers. The preganglionic neurons usually synapse with the postganglionic neurons at the same level, but sometimes go up or down and through one or more ganglia and then synapse.

The neurotransmitter of the preganglionic sympathetic neurons is acetylcholine (ACH). It stimulates action potentials in the postganglionic neurons.

The neurotransmitter released by the postganglionic neurons is noradrenaline (norepinephrine).

The action of noradrenaline on a particular gland or muscle is excitatory in some cases, inhibitory in others.

Messages travel through the SNS in a bidirectional flow. Afferent messages carry sensations such as heat, cold or pain. Efferent messages can simultaneously trigger changes in different parts of the body.

Functions

1. It can accelerate the heart rate, the contractility of the cardiac cells, provide vasodilation for the coronary vessels of the heart, constrict blood vessels and raise blood pressure.
2. It dilates bronchioles of the lung, which allows for greater alveolar oxygen exchange.
3. It decreases motility of the large intestine.
4. It dilates pupils and relaxes the lens, allowing more light to enter the eye.
5. It diverts blood flow away from the gastro-intestinal tract and skin via vasoconstriction.

Thus, it promotes a 'fight or flight' response.

2. Parasympathetic Nervous System (PNS)

The preganglionic outflow of the parasympathetic nervous system arises from the cell bodies of the motor nuclei of the cranial nerves III, VII, IX and X in the brain stem and from the second, third and fourth sacral segments of the spinal cord. It is, therefore, also known as the cranio-sacral outflow.

Preganglionic fibers run almost to the organ that it supplies and synapse in ganglia close to or within that organ. Postganglionic fibers then innervate that organ.

Functions

1. It causes slowing down of the heartbeat and lowering of blood pressure.
2. During accommodation, it causes constriction of the pupil and lens.
3. It dilates blood vessels leading to the GI tract, thus, increasing the blood flow. It increases peristalsis of the GI tract.
4. It constricts the bronchiolar diameter when the need for oxygen has diminished.
5. It is involved in erection of genitals via the pelvic splanchnic nerves.
6. It stimulates salivary glands.
7. It increases blood flow to the skin and viscera.

8. It promotes a 'rest and digest' response, and promotes calming of the nerves to return to regular function.

Thus, the parasympathetic system returns the body functions to normal after they have been altered by sympathetic stimulation. In times of danger, the sympathetic system prepares the body for violent activity. The parasympathetic system reverses these changes when the danger is over.

Table 10.1 *Differences between SNS and PNS*

Sympathetic system	*Parasympathetic system*
Accelerates heart rate	Slows heart rate
Raises blood pressure	Lowers blood pressure
Vasoconstriction	Vasodilatation
Dilates pupil	Constricts pupil
Dilates bronchioles	Constricts bronchioles
Decreases blood flow to skin and viscera	Increases blood flow to skin and viscera
Decreases peristalsis in GIT	Increases peristalsis in GIT

10.2 PHYSIOLOGY

10.2.1 Neurons

The nervous system is made up of a vast number of cells called neurons supported by neuroglia.

A neuron is the structural and functional unit of the nervous system.

A neuron consists of a cell body or soma and two types of processes:

- Dendrites
- Axon

The **cell body or soma** is also known as **perikaryon**. It consists of a cell membrane. The cell has a large nucleus, spherical and centrally situated, which contains the genetic material in the form of chromosomes. It is covered by nuclear membrane. Inside the nucleus, there is nucleoplasm, chromatin network and nucleoli. The cytoplasm is called **neuroplasm** and contains mitochondria and other organelles like neurofibrils, nissle bodies, ribosomes and Golgi apparatus.

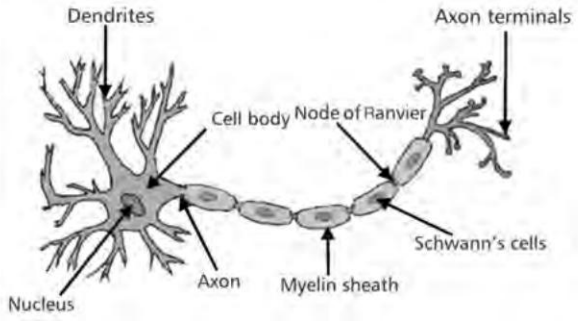


Fig. 10.18 *Structure of a typical neuron*

Neurons differ from other cells in the body in some ways since they have specialized projections—dendrites and axons. **Dendrites** bring information to the cell body while **axons** take information away from the cell body. Neurons communicate with each other through an electrochemical process and contain chemicals called neurotransmitters. Neurons cannot divide and they need a continuous supply of oxygen and glucose for survival.

Neurons have the property of irritability and conductivity.

Irritability is the ability to initiate nerve impulses in response to stimuli, which may come from outside the body, e.g., touch, or from inside the body, e.g., change in the concentration of CO_2 in the blood, which alters respiration.

Conductivity means the ability to transmit an impulse.

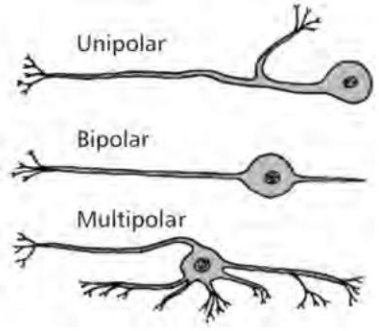


Fig. 10.19 *Types of neurons*

Neurons may be unipolar (only one axon), bipolar (one axon and one dendrite), pseudounipolar (two axons taking origin from the same point) and multipolar (many processes).

Dendrites are many in number and are short processes which are branched and receive impulses. Their structure is the same as the axons. In sensory neurons they are the sensory receptors which respond to stimuli, and in motor neurons they take part in the formation of synapses.

Each nerve cell has only one axon and it carries nerve impulses away from the cell body.

That axon which transmits the impulses towards the spinal cord is known as **sensory or afferent nerve**, and that which transmits the impulses away from the spinal cord is known as **motor or efferent nerve**.

Axons are longer than dendrites, sometimes as long as 100 cm.

An axon arises from the cell body in a conical elevation called **axon hillock**. The centre of the axon, which is tubelike, is known as the **axis cylinder** which contains cytoplasm called **axoplasm**. Axoplasm contains neurofibrils, mitochondria and endoplasmic reticulum. The surface of the axis cylinder is the conducting membrane. The membrane of the axon is called **axolemma**.

Large axons and peripheral nerves are surrounded by a lipid-rich membrane called **myelin sheath**, which is formed by Schwann cells, arranged along the length of the axon.

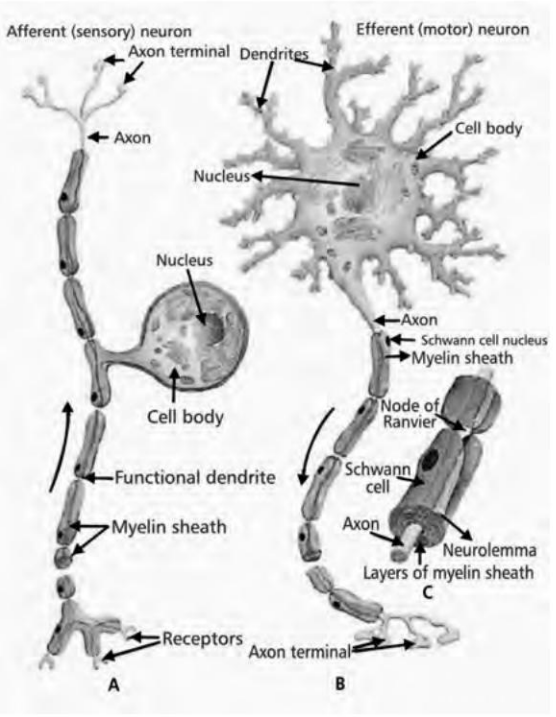


Fig. 10.20 *Neurons—afferent and efferent*

Each one covers a part of the nerve fiber so that it is covered by a number of concentric layers of Schwann-cell plasma membrane. The region where the axon is not covered by myelin sheath is the junction of adjacent myelinated segments, called **node of Ranvier**. They help in the rapid transmission of nerve impulses.

The nerve fibers supplying skeletal muscles are myelinated. Some small fibers in the central nervous system and most of the autonomic nerves are nonmyelinated. Here, transmission is slower.

1. Action Potential

An action potential is a self-regenerating wave of electrochemical activity that allows nerve cells to carry a signal over a distance. Action potentials are generated due to voltage-gated channels, embedded in the plasma membrane. It arises from changes in the permeability of the nerve cell's axonal membranes to specific ions. These channels are closed when the membrane is in the resting state.

In the resting state, the nerve-cell membrane is polarized due to differences in the concentrations of ions across the plasma membrane, i.e., there is a different electrical charge on each side of the membrane. This is called **resting membrane potential**. At rest, the charge on the outside is positive and inside is negative. When the nerve fiber is excited or stimulated by mechanical, chemical or electrical stimulation, certain changes occur and the resting membrane potential is altered. The channels open and there is influx of sodium ions and Na^+ floods into

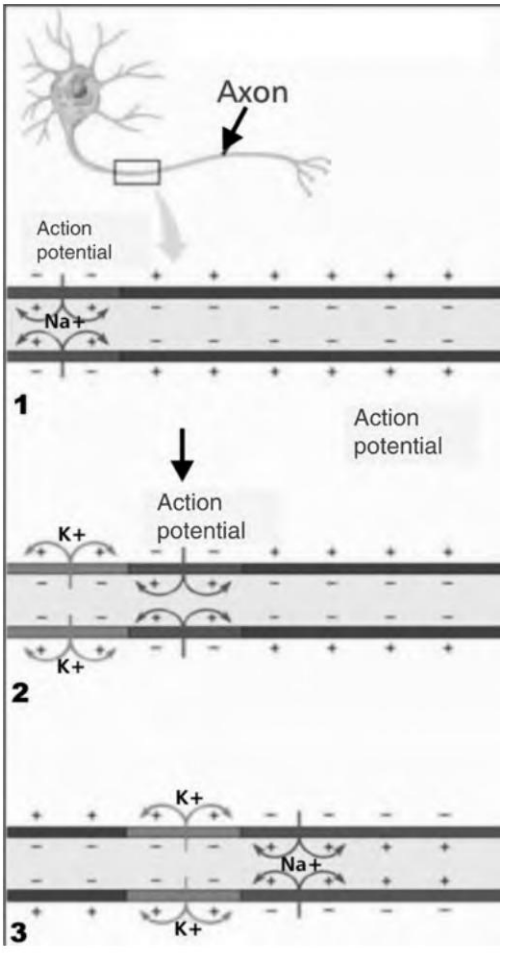


Fig. 10.21 *Action potential (Refer colour figure)*

the neuron from the extracellular fluid, creating a nerve impulse or action potential. Negativity inside is reduced from –90 mV to +35 mV. This process is called **depolarization**. Depolarization is very rapid and impulse passes along the entire length of the nerve in a few milliseconds. Impulse passes in one direction only, i.e., away from the point of stimulation.

As the sodium channels close, they can no longer enter the neuron. They are transported out of the plasma membrane. Potassium channels are now activated and K^+ floods out of the neuron. The electrochemical gradient returns to the resting state. Repolarization process begins after +35 mV. It reaches –65 mV immediately. Then the flow of K^+ ions is reduced. So, negativity from –65 mV to –90 mV reaches slowly. This slow process is called **negative after-potential** or **after-hyperpolarisation**.

After –90 mV, most of the K^+ channels get closed but few remain open which reduces negativity from –90 mV to –100 mV. This is called **positive after-potential**. This movement returns the membrane potential to its resting state.

As the neuron returns to original state, action of sodium pump expels Na^+ from the cell in exchange for K^+. This is the

mechanism which prevents an action potential traveling back the way it just came.

2. Transmission of Nerve Impulse

This single action potential acts as a stimulus to neighboring proteins and initiates an action potential in another part of the neuron.

There are two ways by which the impulse is transmitted in the nerve fiber.

In myelinated neurons, the myelin sheath acts as an effective insulator and prevents movement of ions, so electrical changes across the membrane can occur only at the gaps in the myelin sheath, i.e., nodes of Ranvier. A membrane of the node of Ranvier is 500 times more permeable.

When an impulse occurs at one node, depolarization passes along the myelin sheath to the next node, so that the flow of current appears to leap from one node to the next. This is called **saltatory conduction**.

This type of conduction increases the velocity of impulse transmission in a myelinated nerve fiber and conserves energy. When the 2nd node is depolarized, the 1st node begins to repolarize.

Conduction from receptors to the central nervous system is called **orthodromic conduction**, and from the central nervous system to periphery is called **antidromic conduction**.

Speed of conduction also depends on the diameter of the neuron; larger the diameter, faster the conduction.

Myelinated fibers conduct faster than unmyelinated fibers.

Fastest conduction	130 m/s
Slowest conduction	0.5 m/s

In unmyelinated fibers the flow of current is from point to point. As the action potential develops at one point, the next point gets depolarized and the 1st point repolarizes and the transmission of impulse spreads. As the process of depolarization continues along the membrane in the same way, repolarization follows.

3. Excitation—Conduction Coupling Process

Excitation–conduction coupling process means that an electrical stimulus, which is an action potential, is converted into a mechanical response in the form of contraction.

During normal resting condition, each muscle fiber is –90 mV inside the fiber. This is called a Resting Membrane Potential (RMP).

The axon of the nerve fiber goes distally and divides into many branches. Each branch supplies one muscle fiber. Thus, one nerve fiber supplies one skeletal muscle fiber. Hence there is one neuromuscular junction for each muscle fiber

When impulse reaches the neuromuscular junction, the resting membrane potential is changed into action potential and spreads from the center of the muscle fiber to the various parts of the muscle fiber via the 'T' system.

Spread of action potential causes the release of Ca^+ ions from the sarcoplasmic reticulum into the sarcoplasm.

A large amount of Ca^+ ions remain in the sarcoplasm for 1/30 seconds, which is called **calcium pulse**.

These Ca^+ ions trigger the contraction of skeleton muscle fiber, which is called **excitation–contraction coupling process**.

Here, the coupling agent is the Ca^+ ion.

Details of muscle physiology and neuromuscular transmission are discussed in respective chapters.

4. Neuromuscular Junction

The skeletal muscle fibers are innervated by large myelinated nerve fibers that originate in the large motor neurons of anterior horn cells of the spinal cord.

Each nerve fiber branches many times and innervates from a minimum of three to several hundreds of muscle fibers.

The nerve ending makes a junction with the muscle fiber which is called the neuromuscular junction. It is the union of the axon with the muscle fiber.

There is only one junction for one motor fiber.

The nerve fiber invaginates into the muscle fiber but remains outside the muscle fiber plasma membrane. This entire structure is called **motor-end-plate.**

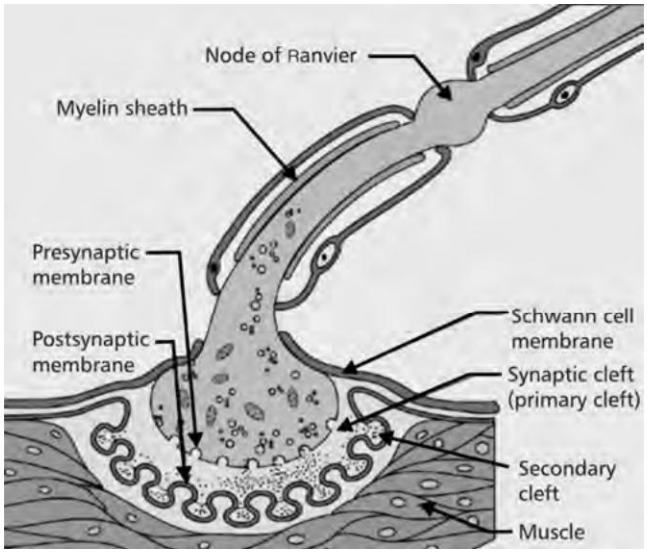


Fig. 10.22 *Neuromuscular transmission*

The space between the nerve terminal and muscle fiber membrane is called **synaptic cleft**.

At the bottom of the gutter are numerous smaller folds of muscle membrane called **subneural clefts**; this increases the surface area at which the synaptic transmitter can act.

In the axon terminal, there are many mitochondria that supply energy, mainly for the synthesis of the excitatory transmitter, acetylcholine.

Acetylcholine is synthesized in the cytoplasm of the terminal, but is rapidly absorbed into many small synaptic vesicles present in the terminal.

The synaptic cleft or space has a fine network of fibers called **basal lamina** and here are large quantities of acetylcholinesterase which is capable of destroying acetylcholine.

When a nerve impulse reaches the neuromuscular junction, the impulse spreads over the terminal; calcium channels open and allow large quantities of Ca^{++} to diffuse to the interior. Ca^{++} ions draw acetylcholine from the vesicles to the neural membrane; some fuse with the neural membrane and empty their acetylcholine into the synaptic space by the process of exocytosis. In the synaptic cleft the acetylcholine combines with the nicotinic receptors on the muscle fiber membrane.

This allows a large amount of Na^{+} ions to pour inside the fiber. The sudden insurgence of Na^{+} ions into the muscle fiber changes the membrane potential in the positive direction from –50 mV to +70 mV, creating a local potential called as **end-plate potential**.

This end-plate potential can initiate action potential in the muscle fiber. When more fibers are activated, it causes muscle contraction.

Released acetylcholine is rapidly removed by two ways:

- Most of the acetylcholine is rapidly destroyed by the enzyme acetyl cholinesterase which is attached to the basal lamina and also lies within the synaptic space.
- A small amount diffuses out of the synaptic space and hence is no longer available for action.

The rapid removal of acetylcholine prevents muscle re-excitation after the fiber has recovered from the first action potential.

Each impulse, which arrives at the neuromuscular junction, causes about three times as much end-plate potential as required to stimulate the muscle fiber.

So, normal neuromuscular junction is said to have a high safety factor. If stimuli come very fast then, release of acetylcholine becomes less and impulses then fail to pass into the muscle fiber. This is called **fatigue of the neuromuscular junction**.

Under normal functioning conditions, fatigue of neuromuscular junction occurs rarely and even then, only at the most exhausting levels of muscle activity.

10.2.2 Synapse

Synapse is a junction which permits a neuron to pass an electrical or chemical signal to another neuron. It is a functional connection between neurons or between neurons and other types of cells. There is always more than one neuron involved in the transmission of a nerve impulse from its origin to its destination. Most synapses connect axons to dendrites, but some presynaptic sites are located on a dendrite or soma. Hence the connections are axon-to-cell-body, axon-to-axon and dendrite-to-dendrite. Synapses are generally too small to be recognizable using a light microscope but their cellular elements can be visualized clearly using an electron microscope.

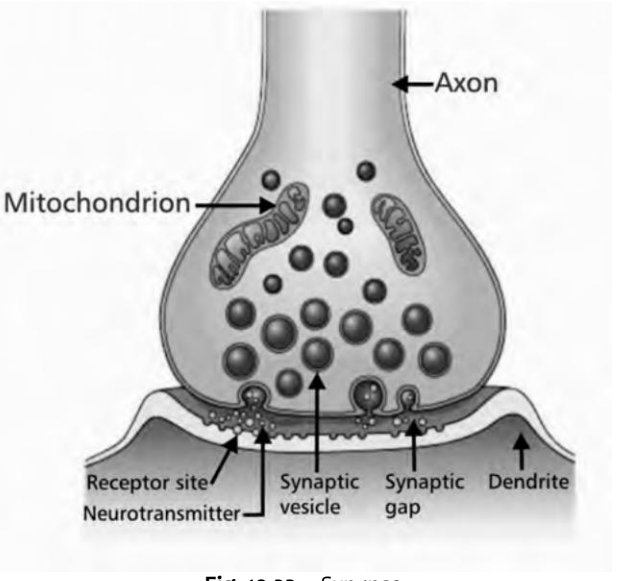


Fig. 10.23 *Synapse*

The presynaptic neuron breaks up into minute branches which terminate in small swellings called **synaptic knobs** or **terminal boutons**. These presynaptic endings contain neurotransmitters, mitochondria and other cell organelles.

Neurotransmitters are synthesized by nerve cells and are actively transported along the axons. They are enclosed in small membrane-bound spheres called synaptic vesicles and are stored there. Between the pre-and post-synaptic cells is a gap called the **synaptic cleft**. The postsynaptic region is found on the dendrites but synapse can occur on axons or the cell body of the next neuron. The membranes of the two adjacent cells are held together by cell-adhesion proteins.

Communication can occur between neurons only when an electrical impulse travels down an axon to the synaptic terminal.

An electrical impulse triggers the migration of vesicles containing neurotransmitters towards the presynaptic membrane. The vesicular membrane fuses with the presynaptic membrane releasing the neurotransmitters into the synaptic cleft. They act on specific receptor sites on the postsynaptic membrane. It changes the postsynaptic cell's excitability. This makes the postsynaptic cell fire an action potential. If the number of excitatory postsynaptic events is big enough, it will cause an action potential to travel down the nerve. Their action is short lived. The cleft allows neurotransmitter concentration to be raised and lowered rapidly. Usually, they are excitatory.

1. Classification

There are two types of classification:

- Functional classification
- Anatomical classification

(a) Functional Classification Functional classification is according to nature of transmission of impulses. It is of two types:

Electrical synapse
Chemical synapse

(i) Electrical Synapse An electrical synapse is an electrically conductive link between two neurons. The membranes of the two communicating neurons come very close at the synapse and are actually linked together by a specialized continuity called the **gap junction**.

The distance between two neurons is 3.5 nm, while it is 20 to 40 nm in chemical synapses.

The postsynaptic potential in electrical synapses is not caused by the opening of ion channels by chemical transmitters, but by direct electrical transmission between both neurons. Action potential is thus transmitted from one neuron to another through this gap junction. Electrical synapses are only used when a reflex is very fast. A benefit of this type of synapse is that the impulse can be transmitted in either direction.

Electrical synapses are faster and more reliable than chemical synapses. They are found throughout the nervous system, but less common than chemical synapses. There is minimal synaptic delay because of direct flow of current.

(ii) Chemical Synapse Chemical synapses are specialized junctions through which neurons signal to each other and to non-neuronal cells like muscles and glands. Almost all the synapses utilized for impulse transmission are of this variety. Gap junctions are absent here. Chemical transmitters are secreted from the presynaptic terminal and act on the postsynaptic neuron. In chemical synapse, transmission of signals is in one direction only.

(b) Anatomical Classification, or Classification According to Nature of Connection The axon of one neuron is in contact with the cell body, dendrite or axon of the next neuron. Depending upon the ending of an axon, the synapse is classified into 3 types.

(i) Axo-somatic Synapse In this type of synapse, the axon of one neuron forms contact with the cell body of the next one.

(ii) Axo-dendritic Synapse Here, the presynaptic terminal (axon) ends on the dendrites of the next neuron, e.g., in the cerebellum.

(iii) Axo-axonic Synapse The axon of one neuron terminates on the axon of another neuron. This type of synapse is not very common.

(iv) Dendro-dendrite Synapse The dendrite of one neuron synapses with the dendrite of the next neuron. It is not common.

Most synapses are axo-somatic and axo-dendritic synapses.

2. Functions

The main function of a synapse is to transmit impulses, i.e., action potential from one neuron to another. But some synapses are inhibitory in function and do not transmit impulses.

Hence, there are excitatory synapses which transmit the impulses and inhibitory synapses which inhibit transmission of impulses.

A wave of electrochemical excitation called an action potential travels along the membrane of the presynaptic cell, until it reaches the synapse. There is depolarization of the membrane at the synapse. Voltage-gated calcium channels in presynaptic membrane are opened. Calcium ions enter the axon terminal, increasing the calcium concentration in the interior. They cause opening of the vesicles and acetylcholine is released by exocytosis. It diffuses within the cleft. Some of it escapes, but some of it binds to chemical-receptor molecules located on the membrane of the postsynaptic cell to form an acetylcholine-receptor complex.

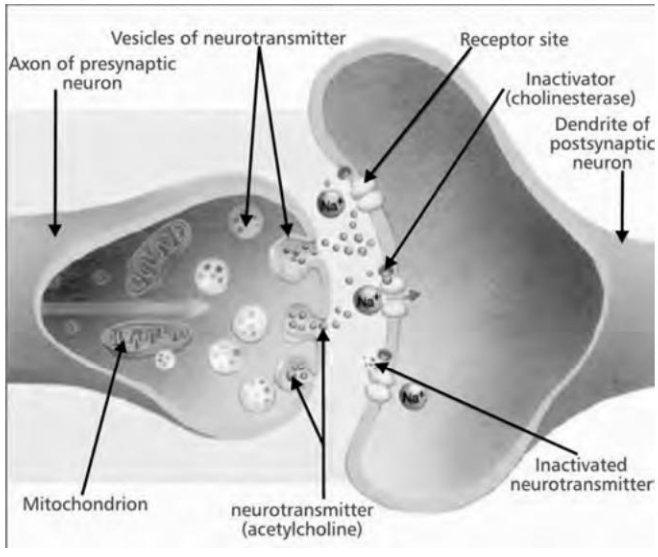


Fig. 10.24 *Impulse transmission at a synapse. The arrow indicates the direction of the electrical impulse*

This complex produces a nonpropagative potential called **Excitatory Postsynaptic Potential** (EPSP). This leads to increase in the permeability to Na^+ and it enters into the soma. The resting membrane potential, inside the soma, is altered and becomes positive and the EPSP leads to the development of action potential. Depolarization occurs in the initial segment of the axon and the action potential, which has developed, spreads further in the axon.

A presynaptic neuron sometimes releases an inhibitory neurotransmitter such as GABA which causes inhibitory postsynaptic potential in the postsynaptic neuron, decreasing its excitability and, therefore, decreasing the neuron's likelihood of firing an action potential. The significance of this type of synapse is that it helps to select the exact number of impulses and omits or blocks excess ones.

10.2.3 Reflex Action

A reflex action is an involuntary instantaneous motor response to a stimulus. Most reflexes do not go up to the brain to be processed, which is why they take place so quickly. Reflex actions are mediated via a very simple nervous pathway, called a **reflex arc**.

Reflexes could be autonomic, conditioned, corneal, conjunctival, spinal or stretch reflex.

When a receptor organ is excited, it sends signals along a sensory neuron to the spinal cord and via the interconnecting neurons; the signals are passed on to a motor neuron. As a result, the effector or efferent organ responds, e.g., when a finger touches a hot surface, a small area of the skin is stimulated and sensations are transmitted to the spinal cord by sensory nerves. They stimulate connector neurons and lower motor neurons in the cord. This leads to contraction of skeletal muscles of the hand, arm and shoulder and there is withdrawal of the finger.

A reflex action takes place very quickly; in fact, the motor response occurs almost instantaneously with the perception of pain. As the integration between afferent and efferent limb occurs at a segment of the spinal cord, this is called **spinal reflex**.

If integration occurs in the brain stem or cerebral cortex, it is called a cerebral reflex.

Classification of Reflexes

Reflexes are classified in four different ways.

(a) First Type of Classification These are inborn or acquired.

(i) Un-conditional Reflex These are inborn reflexes. They are of the following types:

- Superficial
- Deep
- Visceral

They are present since birth and they cannot be changed.

(ii) Conditional Reflex Conditional reflexes are acquired, i.e., they are not present from birth. Thinking, sight, smell of food stimulates secretion in the gastro-intestinal tract.

These reflexes can be established or abolished.

(b) Second Type of Classification This depends on the number of synapses present in the reflex.

(i) Monosynaptic Reflex It is a simple reflex arc of two neurons only.

When the stimulus is given, muscle spindle gets stimulated and there is a response in the form of contraction and movement of a limb, e.g., stretch reflex.

(ii) Disynaptic Reflex In this type of reflex arc, there are three neurons and only one synapse, e.g., tendon reflex.

(iii) Polysynaptic Reflex In this type of reflex arc, there is involvement of several neurons, e.g., withdrawal reflex.

(iv) Complex Reflex Axons of the sensory neurons, while passing upwards in the spinal cord, give branches at different segmental levels and each of the co-lateral branch forms a separate reflex arc.

(c) Third Type of Classification This is anatomical classification.

(i) Segmental Reflex In segmental reflex, an arc is formed at a particular segment of the spinal cord.

(ii) Intersegmental Reflex In intersegmental reflex, different segments of the spinal cord are involved in the formation of this reflex, e.g., withdrawal reflex.

(iii) Suprasegmental Reflex This reflex involves neurons above each corresponding segment of the spinal cord. The integrating part extends from spinal cord up to the brain, e.g., postural reflex, labyrinthine reflex.

(d) Fourth Type of Classification This is clinical classification.

(i) Superficial Reflexes Stimulus is applied on the superficial part of the body, e.g., on skin, mucous membrane, cornea or conjunctiva and the necessary response is obtained. They are of the following types: corneal, conjunctival, palatopharyngeal, abdominal, anal, cremasteric and plantar.

Plantar reflex is also called pathological reflex or **Babinski positive**.

Normally, when stimulus is applied to the skin of the sole of a foot, it is stretched and there is flexion of all toes—**Babinski negative**.

But if response is dorsiflexion of the great toe and fanning of the other toes then it is called Babinski positive. Normally, this occurs in deep sleep and in children. But when there is upper motor neuron lesion, it is pathological.

(ii) Deep Reflexes They are mainly stretch reflexes, also known as tendon reflexes.

Application of stimulus is to the deeper part of the body.

They are of the following types: jaw jerk, biceps jerk, triceps jerk, supinator jerk, knee jerk and ankle jerk.

The cell body of lower motor neuron is stimulated by the sensory neuron. No connector neuron is involved here, e.g., in knee jerk, the tendon below the knee is tapped and thigh muscles are stretched. So a nerve impulse passes to the spinal cord and the cell body in the anterior column of gray matter on the same side sends messages to the thigh muscles which contract and the leg is kicked forward.

This type of reflex has a protective function. It prevents excessive joint movement that may damage tendons, ligaments and muscles.

(iii) Visceral Reflexes, also called Autonomic Reflexes

An autonomic reflex is one that involves the response of an organ that is not controlled consciously. Autonomic reflexes occur over autonomic reflex arcs.

Components of that reflex arc are a sensory receptor, sensory neuron, integrating center, pre and postganglionic motor neuron and visceral effector organ.

Autonomic reflex arcs are vital for important functions, such as gut peristalsis, sweating, etc., and for the most part, these activities are carried out without conscious thought or volition.

They are micturition reflex, defecation reflex, vascular reflex, baroreceptor reflex, respiratory reflex, digestive reflex, sexual reflex and pupillary reflex.

10.2.4 Sensations

A sensation means the feeling aroused by a change in the environment, which is transmitted to the central nervous system and by which the person remains aware of the surroundings. Special endings of sensory neurons respond to the changes (stimuli) inside and outside the body.

Classification

There are mainly two types of sensations:

- Somatic sense
- Special sense

(a) Somatic Sense Sensations arising from the skin—such as touch, pressure, cold, warmth, and pain—and from the muscles, tendons, and joints—such as the position of the limbs and pain—are known as somatic sensations.

Somatic sense can be classified in two ways:

(i) First Group of Classification

(A) **Mechanoreceptive somatic sense**

Here, the sensations are produced by mechanical displacement of some tissue of the body.

1. *Tactile sense* (fine touch) where there is simple contact of body and *crude touch*, which detects degree of force acting on skin and subcutaneous tissue.
2. *Kinesthetic / proprioceptive somatic sense*

It is the sensation aroused from muscles, tendons, joints.

Conscious kinesthetic impulses are joint sense, sense of vibration and sense of position.

Unconscious kinesthetic impulses are impulses for muscle tone and sense for tension of muscles.

(B) Thermo receptive somatic sense

It detects the sensation of heat and cold, pain / nociceptive somatic sense.

It is activated by any factor which damages the tissue.

(ii) Second Group of Classification

1. **Superficial/exteroceptive sensation**
   Sensations aroused from superficial parts of the body like skin, subcutaneous tissue, conjunctiva and mucous membrane are included in this group.
2. **Deep sensations/proprioceptive sensation**
   They arise from muscles, tendon or joints.
   It is of two types:
   Conscious—Joint sense, sense of vibration and position
   Unconscious—Muscle tone and muscle tension
3. **Visceroceptive sensations**
   Sensations arising from the viscera such as pain or the sense of fullness of the stomach or bladder are considered as visceral sensations. Pain arising from the viscera is often felt as if it comes from some other part of the body surface or underlying tissue. This is called referred pain. (See Fig. 10.25)
4. **Cortical sensations**
   Though they arise from a superficial part of the body, they are analyzed at the sensory cortex only.

They are

1. *Tactile localization*—ability to locate the touch
2. *Tactile discrimination*—ability to differentiate two touches applied simultaneously on the body
3. *Stereognosis*—ability to detect the object by size and shape with closed eyes by touch; inability to do it is called astereognosis

(b) Special Senses The special senses are sound, sight, smell and taste which have special organs for each.

They are discussed in detail in respective chapters.

10.2.5 Receptors

A receptor is a structure on the surface of a cell or embedded in either the plasma membrane or the cytoplasm of a cell that selectively receives and binds a specific substance. Physiologically, they can be defined as specialized cells or a group

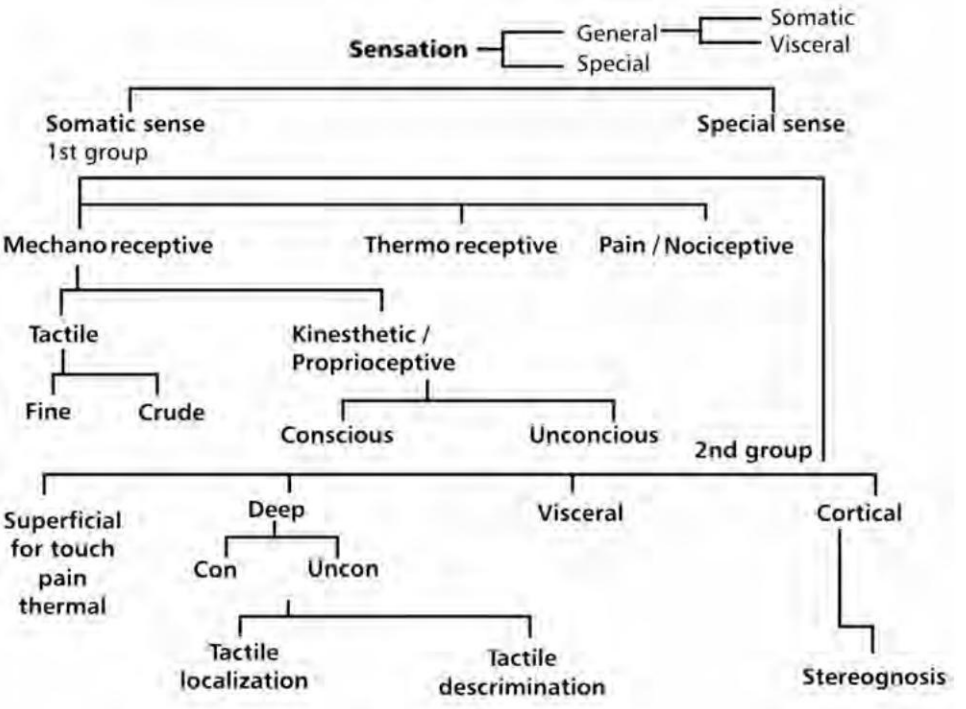


Fig. 10.25 *Summary of classification of sensations*

of nerve endings that respond to sensory stimuli. A molecule which binds to a receptor is called a ligand which may be either a peptide or other small molecule such as a neurotransmitter, a hormone, a toxin or a drug.

Receptors enable the body to detect changes in the internal or external environment. All sensory nerve endings function as receptors. In response to stimuli, the sensory receptor initiates or creates graded potentials or action potentials in the same cell or in an adjacent one.

Classification according to location

- Exteroreceptors
- Interoreceptors

(a) Exteroreceptors These respond to stimuli coming from outside the body. They are the following:

(i) Cutaneous Receptors They are sensory receptors found in the dermis or epidermis. They respond to mechanical stimuli like pain, touch and pressure. They are a part of the somatosensory system. Cutaneous receptors include cutaneous mechanoreceptors, nociceptors (pain) and thermoreceptors (temperature).

The sensory receptors in the skin are

- **Cutaneous mechanoreceptors**
  - — Ruffini's end organ (heat)
  - — Meissner's corpuscle (touch)
  - — Pacinian corpuscle (deep pressure, vibrations)
  - — Merkel's disc (sustained touch and pressure)
  - — Free nerve endings (pain)
- **Thermo receptors** are sensitive to temperature changes.
- **Nociceptors** are activated by intense stimuli that may damage tissue.

Sensation produced is pain.

(ii) Chemoreceptors They respond to chemical stimuli. They are stimulated by various changes in chemical composition. These are taste buds for taste and olfactory receptors for recognizing smell.

(iii) Telereceptors They are specialized sense receptors such as those in the eyes, ears and nose, which respond to distant external stimuli. An organ such as the eye can receive sensory stimuli (of vision) from a distance. Rods and cones found in the retina are telereceptors and are also called visual receptors or photoreceptors or electromagnetic receptors.

The hair cells of the organ of Corti are the receptors in the ears.

Olfactory neurons in the nose and gustatory cells of taste buds in the tongue act as telereceptors.

(b) Interoreceptors They maintain internal body conditions. They detect internal stimuli and convey information about the internal environment. For example, interoreceptors in the arteries detect changes in the blood pressure.

They are of two types:

- Visceroreceptors
- Proprioceptors

Visceroreceptors These are located in the smooth muscles of blood vessels and viscera. They provide information about the internal environment.

They are of the following types:

(a) **Baroreceptors** detect changes in the pressure. They are present mainly in the carotid sinus and the aortic arch.

(b) **Chemoreceptors** respond to chemical changes and are present in carotid body and aortic body.

(c) **Osmoreceptors** respond to changes in the osmotic pressure in the body and regulate water balance and osmotic pressure. They are present in the brain and hypothalamus.

(d) **Stretch receptors** They respond to stretch and are present in the lungs and hollow viscera. Glucoreceptor in hypothalamus and central chemoreceptor in the brain stem are also examples of this.

(c) Proprioceptors They are special nerve endings in the muscles and tendons and other organs that respond to stimuli regarding change in the position and movement of the body. They are also called the receptors of kinesthetic sensation and are situated in the labyrinth, muscles, joints, ligaments and fascia. They are the source of the perception of one's own body position and movement.

The proprioceptors are

- Muscle spindle
- Golgi tendon organ
- Pacinian corpuscle
- Free nerve ending
- Proprioceptors in the labyrinth

1. Histological Classification

(a) Uncapsulated Receptors

(i) Free Nerve Endings They are simple, undifferentiated, terminal ends of sensory nerve fibers.

(ii) Merkel's Disks It is an expanded tip of tactile receptor.

(iii) Hair-end Organ They surround the base of the hair follicle in the form of short vertical filaments.

(b) Capsulated Receptors

They are specialized sensory end organs enclosed in a connective tissue capsule.

(i) Meissner's Corpuscles They are seen inside the capsule and in nonhairy parts of the skin.

(ii) Pacinian Corpuscles They are found in the subcutaneous tissue and near the tendons and joints.

(iii) Krause's End Bulbs They are found in dermis and subcutaneous tissue, mucous membrane and joint capsule.

(iv) Raffini's Capsule They are located in the deeper tissues.

(v) Golgi Tendon Organ They are for motor activity.

(vi) Muscle Spindle They are for reflex control.

Classification by Stimulus that causes Response

1. Mechanoreceptors
2. Chemoreceptors
3. Thermoreceptors
4. Nociceptors
5. Photoreceptors

2. Properties of Receptors

(a) Specificity of Response Each receptor responds to a particular type of stimulus, viz., the pain receptors are stimulated by pain stimulus. Chemical substances stimulate chemoreceptors.

(b) Adaptation When a receptor is continuously stimulated with the same strength of stimulus over a period of time, it leads to a decreased rate of impulse conduction and a decreased intensity of sensation. The receptor adapts. This property is called adaptation.

Adaptation is of the following types:

(i) Rapid Adapting Receptor Phasic receptors get adapted rapidly. They are the touch and pressure receptors. They give information about the changing position of the body to the brain and react only when kinetic change takes place rather than static change.

(ii) Slowly Adapting Muscle spindle, pain receptors, cold receptors, chemoreceptors are tonic receptors which adapt slowly.

They give information to the brain regarding the static condition of the body.

(iii) Non-adapting They are protective receptors. The best example is the pain receptors.

(c) Response to Increase in Strength of Stimulus The strength of the stimulus must be increased 100 times if the response given by the receptor is to be doubled. This phenomenon is called **Weber Fechner law**.

(d) Receptor Potential Receptor potential is the transmembrane potential difference of a sensory receptor.

When a receptor is stimulated, a nonpropagated depolarization occurs. There is sudden opening of Na^+ channels causing entry of Na^+ ions inside. This creates positivity inside. This is the receptor potential. It is comparable to the EPSP in synapse or the neuromuscular junction.

(e) Control of Receptor Receptors are controlled by the central nervous system. The activity of receptor is altered by efferent impulses coming from CNS.

(f) Recruitment When sensory stimulation is weak, a small area is stimulated and when signals are strong, large area and high threshold receptors are stimulated.

(g) Inhibition Excessive number of tactile sensation reduces transmission of pain signals.

10.2.6 Electroencephalography

Electroencephalograph (EEG) is the recording of electrical activity as recorded from electrodes placed on the scalp, produced by the current generated in the neurons within the brain. It is a non-invasive test. It is generated by the changes in the electrical charge of the membrane of the cortical nerve cells. Electroencephalography is the technique and electroencephalogram is the instrument which records the electrical activity.

Clinical Applications

1. The main diagnostic application of EEG is in cases of epilepsy, as epileptic activity causes abnormalities and marked discharges are seen on standard EEG studies. It is the investigation of choice for patients presenting with paroxysmal convulsive disorders or epileptic disorders. It is also useful as a guideline to judge the progress, so that line of treatment can be monitored.

   In **grandmal epilepsy**, EEG shows high-voltage waves occurring 8 to 12 times per second during the tonic phase and slower waves are seen during the clonic phase. In **petitmal epilepsy**, EEG shows spike and round waves occurring 3 times a second. In **psychomotor type**, the EEG pattern shows low frequency of rectangular waves occurring 2 to 4 times a second.

   EEG helps to distinguish epileptic seizures from other types of convulsive movement disorders and syncope.

   It also helps decide about the weaning of anti-epileptic medications.
2. Electroencephalography is also useful in localizing structural abnormalities such as space occupying lesions—brain tumor.

   But the use of this investigation is becoming limited with the advent of anatomical imaging techniques such as MRI and CT.
3. It is useful to prognosticate in patients of coma and encephalopathies.
4. It plays a very important role in evaluating patients with an altered level of consciousness.
5. It is used to study natural sleep.
6. EEG study serves as an adjunct of brain death.
7. It can also be used in intensive care units for brain-function monitoring.
8. It is useful in cases of increased intracranial pressure. Delta waves with amplitudes up to 100 microvolts are seen and the frequency is 3 per second.

Procedure

EEG examination is done in a quiet place with the patient relaxed, either seated or lying comfortably, with eyes closed.

Winning the confidence of the patient is very important especially, as a good number of patients are children. The procedure is explained to the patient and relatives. The patient has to be totally relaxed and may have to be sedated.

The procedure is carried out for 30 to 40 minutes.

The hairs have to be washed thoroughly.

The EEG is recorded by placing electrodes on the scalp. The electrodes are coated with a conductive paste or gel. They are held in position by adhesives, suction or pressure from caps or headbands.

Fig. 10.26 *A patient undergoing EEG procedure*

Alternatively, needle electrodes are placed but they are very rarely used.

Some use caps or nets into which electrodes are embedded; this is particularly common when high-density arrays of electrodes are needed.

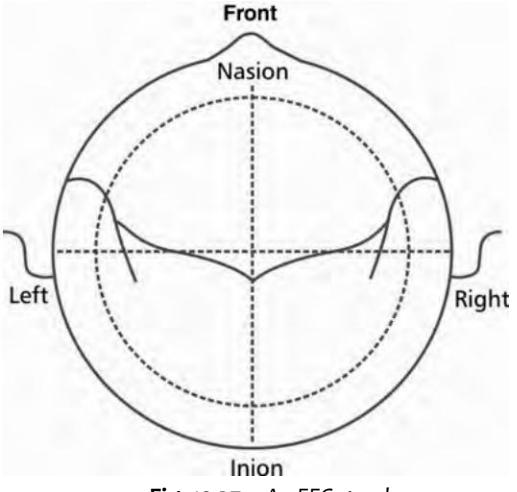


Fig. 10.27 *An EEG graph*

These standard set of electrodes are placed according to specific fixed bony landmarks or positions.

The four standard positions are

- Nasion
- Inion
- Right and left pre-auricular points

Electrode locations and names are specified by the International 10–20 system.

The electrical signals from the brain are converted into wavy lines. The potential differences between the electrodes are amplified and recorded on a continuously moving paper by a number of pen writers, which record these waveforms.

Traces from the right side of the head are displayed above those from the left, and those from the anterior part of the head are displayed above those from the most posterior areas.

Besides these routine electrodes, there are special electrodes for recording the activity of inaccessible regions of the brain because activity here may not be detected by the electrodes placed on the scalp.

These special electrodes are the following:

(a) Nasopharyngeal Electrode A flexible insulated rod with a small silver electrode at the tip is inserted into the nostril till the tip is in contact with the mucosa of the posterior nasopharynx.

It records activity from the anteromedial surface of the temporal lobe.

(b) Sphenoidal Electrodes A sterile needle or fine wire, which is insulated except at the tip, is inserted percutaneously under local anesthesia, so that it lies adjacent to the sphenoid bone.

During the recording, a series of activation procedures are carried. These procedures may induce normal or abnormal EEG activity that might not otherwise be seen. These procedures include hyperventilation, photic stimulation (with a strobe light), eye closure, mental activity, sleep and sleep deprivation.

(i) Eye Closure During the recording the patient is asked to open the eyes for a few seconds and then again close them.

(ii) Hyperventilation Patient is asked to take deep and rapid breaths for 3 to 4 minutes.

EEG is recorded during the period of hyperventilation and for the following 2 minutes. The eyes are generally kept closed during the procedure.

(iii) Sleep or Sleep Deprivation The sleep EEG uses the same equipment and procedures as a regular EEG. Patients are encouraged to fall asleep completely. They are provided a bed and a quiet room conducive to sleep. A sleep EEG lasts up to three hours.

Sleep deprivation also produces EEG abnormalities. These procedures are carried out only in specific conditions.

Photic Stimulation EEG is recorded during photostimulation. EEG is recorded with eyes open for 5 seconds and then for 5 seconds while eyes are closed.

The EEG is described in terms of rhythmic activity and transients. The rhythmic activity is divided into bands by frequency. Four major types of continuous rhythmic EEG waves are recognized, viz., alpha, beta, theta, and delta.

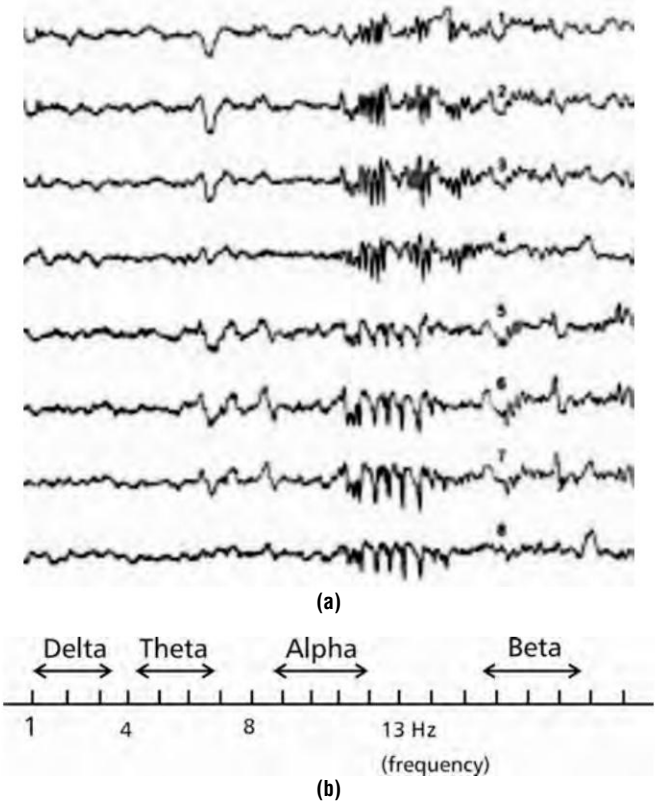


Fig. 10.28 *EEG Waveforms*

- The **alpha rhythm** has a frequency of between 8 and 13 Hz.

The alpha rhythm is dominant over the posterior portions of the head during wakefulness and is best seen when the patient is resting with eyes closed. It attenuates with eye opening. Amplitude is generally 20–100 mV.

It is rhythmic, regular, waxing and waning.

Slowing of alpha rhythm occurs with age.

Slowing is also seen with certain medicines like anticonvulsant drugs and in patients with clouding of consciousness, metabolic disorders or cerebral pathology.

Alpha rhythm increases in frequency in children as they mature and in older patients who are thyrotoxic.

- **Beta activity** has a frequency of greater than 13 Hz, common being 18–25 Hz, less common being 14–16 Hz

and rarely 35–40 Hz. Amplitude usually is in the range of 5–20 mV.

It is mostly seen in the frontocentral region but is somewhat variable; some describe various types according to location and reactivity like generalized, precentral and posterior.

It is usually rhythmic, waxing / waning and symmetric.

It is regarded as a fast variant of alpha rhythm.

It fails to respond to eye opening.

It may be induced by a number of different drugs, especially barbiturates and benzodiazepines compounds.

In localized brain pathology, there may be focal or lateralized spontaneous activity.

Beta activity is enhanced during stages I and II of sleep and tends to decrease during deeper stages of sleep.

Generalized paroxysmal fast activity is seen in 20% of those who have seizure disorders and most of them also have mental retardation.

- **Theta activity** has a frequency of 3.5 to 7.5 Hz and is classed as slow activity. It is seen in connection with daydreaming and fantasizing. Theta waves are strong during internal focus, meditation, prayer and spiritual awareness. It reflects the state between wakefulness and sleep and is related to the subconscious. It is abnormal in awake adults but is perfectly normal in children up to 13 years of age. Hence, presence of theta activity in adults has great significance. It is also normal during sleep.

  Theta activity is believed to reflect activity from the limbic system and hippocampal regions. Theta activity is observed in anxiety, behavioral activation and behavioral inhibition.

  Focal or lateralized theta activity is commonly seen in cerebral pathology.
- **Delta activity** has lowest frequencies. Activity slower than 4 Hz is called delta activity and occurs in deep sleep. Delta waves are involved with our ability to integrate and let go. It reflects the unconscious mind.

  It is the dominant rhythm in infants up to one year of age and it is present in stages 3 and 4 of sleep.

  When delta activity is present in the EEG of awake adults, it is a definite indication of abnormality.

These 4 waves are the normal rhythm patterns seen in a normal patient.

But sometimes even in normal subjects, certain **variations** are seen.

1. A number of normal subjects may have a generally low-voltage EEG.
2. During drowsiness and light sleep, runs of positive spikes may occur superimposed on slower waves.
3. In 25 % of normal adults, small sharp spikes or benign epileptic form transients of sleep are seen during drowsiness or light sleep.

Bursts of rhythmic sharp theta waves with a notched appearance may be seen in young adults.

EEG Changes with Aging The most common finding is slowing of alpha frequency.

It is also seen that intellectual decline and slowing of alpha rhythm has an association.

Effect on beta activity is less clear.

Diffuse theta and delta activity is significantly increased in elderly persons and is clearly related to deterioration in intellectual and life expectancy.

10.2.7 Sleep

Sleep is the natural state of bodily rest. It is a refreshing, peaceful state, devoid of stress. It is distinguished from wakefulness by a decreased ability to react to external stimuli and it is easily reversible. A sleeping person is unconscious to most things happening in the environment. The biggest difference between someone who is asleep and someone who has fainted or gone into a coma is the fact that a sleeping person can be aroused by a harmless stimuli and by a stimulus strong enough, e.g., if you shake the person, yell loudly or flash a bright light. Sleep is needed for restoring brain function which is essential for normal brain activity. A good night's sleep helps maintain physical, mental, social and academic health. Sleeping habit and rhythm differs from person to person and also depends on age. Normal sleep requirement in adults is 7–9 hours. Children need more sleep per day than adults to develop and function properly.

Sufficient sleep benefits alertness, memory, problem solving, and overall health, as well as reducing the risk of accidents. Cognitive performance declines with six or fewer hours of sleep.

Sleep difficulties are closely associated with psychiatric disorders such as depression, alcoholism and bipolar disorder. Up to 90% of patients with depression are found to have sleep difficulties.

Nerve-signaling chemicals called neurotransmitters control whether we are asleep or awake by acting on different groups of nerve cells, or neurons, in the brain.

1. Stages of Sleep

Sleep is divided into two broad types:

Non-Rapid Eye Movement (NREM or non-REM) sleep or slow wave sleep and

Rapid Eye Movement (REM) sleep:

Each type has a distinct set of associated physiological, neurological, and psychological features.

Non-rapid eye movement sleep is dreamless sleep. 80% of sleep is NREM sleep. It is divided into 4 stages:

- Stage I is drowsiness.

- Stage II is light sleep.
- Stage III is profound sleep.
- Stage IV is deep sleep.

Stage I shows transition from alpha waves to theta waves. It is light sleep or somnolance, and the person drifts in and out of sleep and can be awakened easily. Many also experience sudden muscle contractions called **hypnic myoclonia**. These sudden movements are similar to the 'jump' made when startled.

Stage II is characterized by bursts of rapid waves called **sleep spindles** ranging from 12 to 16 Hz. During this stage, muscular activity decreases, eye movements stop and conscious awareness of the external environment disappears. Brain waves become slower. This stage occupies 45 to 55% of total sleep in adults.

Stage III is characterized by slow brain waves called delta waves ranging from 0.5 to 4 Hz (also called delta rhythms). This is the stage in which parasomnias as night terrors, bedwetting, sleepwalking, and sleep-talking occur.

Stage IV shows delta waves almost exclusively.

It is very difficult to wake someone during stages 3 and 4, which together are called deep sleep. There is no eye movement or muscle activity. People awakened during deep sleep do not adjust immediately and often feel groggy and disoriented for several minutes after they wake up.

Sleep stages are assessed by polysomnography in a specialized sleep laboratory. Measurements taken include electroencephalography (EEG) of brain waves, electrooculography (EOG) of eye movements, and electromyography (EMG) of skeletal muscle activity. Each sleep cycle lasts from 90 to 110 minutes and each stage may have a distinct physiological function. Drugs such as sleeping pills and alcoholic beverages can suppress certain stages of sleep, leading to sleep deprivation.

Physiological activities show changes in the form of more secretion of growth hormone, slow and regular breathing and pulse rate, relaxation of skeletal muscles and there is no eye movement.

Rapid eye movement sleep, or REM sleep, accounts for 20–25% of total sleep time in normal human adults. REM sleep plays a crucial role in learning by consolidating the memories of the preceding day and by eliminating unnecessary recollections from the brain. It is classified into **tonic** and **clonic** phases.

When switched into REM sleep, breathing becomes more rapid, irregular, and shallow, eyes jerk rapidly in various directions, and limb muscles become temporarily paralyzed. Heart rate increases, blood pressure rises, and males develop penile erections. It starts within 90 minutes from the onset of sleep. It is characterized by a rapid low-voltage EEG.

When people awaken during REM sleep, they often describe bizarre and illogical tales—dreams.

The first sleep cycles, each night, contain relatively short REM periods and long periods of deep sleep. As the night progresses, REM sleep periods increase in length while deep sleep decreases.

Pathophysiology Sleep timing is controlled by the circadian clock, sleep–wake homeostasis, and in humans, within certain bounds, willed behavior. The circadian clock—an inner timekeeping, temperature-fluctuating, enzyme-controlling device—works in tandem with adenosine, a neurotransmitter that inhibits many of the bodily processes associated with wakefulness. Adenosine is created over the course of the day. High levels of adenosine lead to sleepiness. Sleepiness occurs as the circadian element causes the release of the hormone melatonin and a gradual decrease in core body temperature. The timing is affected by one's chronotype. It is the circadian rhythm that determines the ideal timing of a correctly structured and restorative sleep episode.

Many people have a temporary drop in alertness in the early afternoon, commonly known as the 'post-lunch dip' or siesta. While a large meal can make a person feel sleepy, the post-lunch dip is mostly an effect of the biological clock.

2. *Benefits of Sleep*

There are multiple arguments supporting the restorative function of sleep. Body is rested after sleeping, and it is natural to assume that this is a basic purpose of sleep.

Wound healing has been shown to be affected by sleep.

Sleep maintains the immune system. It has been shown that sleep deprivation affects the immune system.

It has yet to be proven that sleep duration affects somatic growth. It has been shown that sleep—more specifically, slow-wave sleep (SWS)—does affect growth-hormone levels in adult men. During eight hours' sleep, the men with a high percentage of SWS had high growth-hormone secretion, while subjects with a low percentage of SWS had low growth-hormone secretion.

The metabolic phase during sleep is anabolic. Anabolic hormones such as growth hormones (as mentioned above) are secreted preferentially during sleep.

Non-REM sleep may be an anabolic state marked by physiological processes of growth and rejuvenation of the person's immune, nervous, muscular, and skeletal systems. Wakefulness may, perhaps, be viewed as a cyclical, temporary, hyperactive catabolic state during which the organism acquires nourishment.

According to the ontogenetic hypothesis of REM sleep, REM sleep appears to be important for development of the brain. REM sleep occupies the major part of sleep of infants, who spend most of their time sleeping.

However, this does not explain why older adults still need REM sleep.

Sleep is related to memory. Working memory was shown to be affected by sleep deprivation, which is important because it keeps information active for further processing and supports higher-level cognitive functions such as decision making, reasoning, and episodic memory.

3. Drugs and Sleep

Alcohol, barbiturates, melatonin and trytophan are sleep depressants. Amphetamines, caffeine and cocaine are stimulants. Heavy smokers sleep lightly and have reduced amount of REM sleep due to the effect of nicotine.

4. Dreaming

Dreaming is the perception of sensory images and sounds during sleep, in a sequence which the dreamer usually perceives more as an apparent participant than an observer. Dreaming is stimulated by the pons and mostly occurs during the REM phase of sleep. We typically spend more than 2 hours each night dreaming. Scientists do not know much about how or why we dream.

5. Sleep and Disease

Sleep and sleep-related problems play a role in a large number of human disorders and affect almost every field of medicine. For example, problems like stroke and asthma attacks tend to occur more frequently during the night and early morning, perhaps due to changes in hormone levels, heart rate, etc.

Sleep deprivation also triggers seizures in people with some types of epilepsy.

Neurons that control sleep interact closely with the immune system. Infectious diseases tend to make one feel sleepy. This probably happens because cytokines, chemicals that the immune systems produce while fighting an infection, are powerful sleep-inducing chemicals.

Sleeping problems occur in almost all people with mental disorders, including those with depression and schizophrenia.

Sleeping problems are common in many other disorders as well, including Alzheimer's disease, stroke, cancer and head injury.

6. Sleep Disorders

Disorders include insomnia, sleep apnea, restless-legs syndrome and narcolepsy.

(a) Insomnia Almost everyone occasionally suffers from short-term insomnia. This problem can result from stress, jet lag, diet or many other factors. Insomnia almost always affects job performance and well-being the next day.

(b) Sleep Apnea Sleep apnea is a disorder of interrupted breathing during sleep. It usually occurs in association with fat build-up or loss of muscle tone with aging. These changes allow the windpipe to collapse during breathing because muscles are relaxed during sleep. This problem, called **obstructive sleep apnea**, is usually associated with loud snoring (though not everyone who snores has this disorder). In some high-risk individuals, sleep apnea may even lead to sudden death from respiratory arrest during sleep.

(c) Restless-Legs Syndrome Restless-Legs Syndrome (RLS), a familial disorder, causing unpleasant crawling, prickling, or tingling sensations in the legs and feet gives an urge to move them for relief. It is emerging as one of the most common sleep disorders, especially among older people. It may be linked to other conditions such as anemia, pregnancy, or diabetes.

(d) Narcolepsy People with narcolepsy have frequent 'sleep attacks' at various times of the day, even if they have had a normal amount of night-time sleep. These attacks last from several seconds to more than 30 minutes. People with narcolepsy also may experience cataplexy (loss of muscle control during emotional situations), hallucinations and temporary paralysis when they awaken. The disorder (or at least a predisposition to it) is usually hereditary, but it is occasionally linked to brain damage from a head injury.

10.2.8 Speech

Speech is a form of human communication of ideas, where during expiration the sounds produced by the vocal cords are manipulated by the contraction of the muscles of the cheeks and throat and movement of the tongue and lower jaw. It is a higher faculty for expression of feelings, meanings and thoughts. The anatomy, physiology and therefore its pathology is not completely understood.

Speech areas are located in the dominant hemisphere, which is usually the left one, but in left-handed persons it is in the right hemisphere or it may, even, be located bilaterally. The Broca's area is important for verbal expression and is located in the 3rd frontal convolution. The Wernicke's area is important in understanding of received speech and for selection of words to express ideas.

Speech is learnt in childhood and for this, hearing should be totally normal. Listening to speech begins at 6 months of age. Spoken language begins at the age of 9 months. The child mimics the sounds he hears and associates them with objects or meaning.

Speech disorders could be in the form of dysplasia, dysarthria, word deafness and word blindness.

10.2.9 Neurotransmitters

Neurotransmitters are chemical agents that are synthesized by neurons and stored in their terminals. They transmit signals

from a neuron to a target cell across a synapse. The substances released may act locally—nerve or muscle—or at distant organs. They are also produced by some glands like the pituitary and the adrenal glands.

Details of release and action on nerves and muscles have been discussed with synapse and neuromuscular junction.

The different neurotransmitters are noradrenaline, acetylcholine, dopamine, GABA, serotonin, glutamate and endorphin.

There are, however, other neurotransmitters, such as acetylcholine, for which both excitatory and inhibitory receptors exist; and there are some types of receptors that activate complex metabolic pathways in the postsynaptic cell to produce effects that cannot appropriately be called either excitatory or inhibitory. Thus, it is an oversimplification to call a neurotransmitter excitatory or inhibitory—nevertheless it is convenient to call glutamate excitatory and GABA inhibitory.

1. Types

The direct effect of a neurotransmitter depends on the property of the postsynaptic receptor. For some neurotransmitters, the receptors have excitatory effect. Glutamate is excitatory. For other neurotransmitters such as GABA, receptors have inhibitory effect. For neurotransmitters like acetylcholine, both excitatory and inhibitory receptors are present. Hence, neurotransmitters are classified into excitatory and inhibitory neurotransmitters.

(a) Excitatory Neurotransmitters A neurotransmitter is called excitatory when impulse passes from presynaptic neuron to postsynaptic neuron or receptor, leading to depolarization of the membrane and promotes action potential generation. There is change in the resting membrane potential. Sodium channels open, leading to influx of sodium. Excitatory postsynaptic potential develops which in turn causes development of action potential.

Acetylcholine and dopamine are common excitatory neurotransmitters.

(b) Inhibitory Neurotransmitters A neurotransmitter is called inhibitory when the activation of the receptor causes hyperpolarisation which depresses action-potential generation. The neurotransmitter causes opening up of potassium channels leading to influx of potassium in the postsynaptic membrane. Inhibitory postsynaptic potential develops which is called **hyperpolarisation**. Action potential does not develop.

Gamma Amino Butyric Acid (GABA) and dopamine are common inhibitory neurotransmitters.

(i) Noradrenaline Noradrenaline or norepinephrine is a catecholamine and acts as a neurotransmitter and a hormone. It is released following stressful events leading to a host of physiological changes. It is released from the postganglionic fibers of the sympathetic nervous system.

Adrenal medulla releases norepinephrine into the blood. Other sites of its release are the cerebral cortex, brain stem, hypothalamus, locus ceruleus in the pons and spinal cord. Most of the time, it is excitatory but, in a very few places, it causes inhibition. It causes elevation of mood and sexual arousal.

It is synthesized by a series of enzymatic steps, both in the adrenal medulla and the postganglionic nerves, from the amino acid tyrosine. The precursor is phenylalanine which is converted into tyrosine by the enzyme hydroxylase. Tyrosine is hydrolyzed by the enzyme tyrosine hydroxylase into dihydroxy-phenylalaline or DOPA. DOPA is converted into dopamine by the enzyme decarboxylase. Dopamine is taken up by the granules and is converted into noradrenaline by dopamine beta-hydroxylase. Noradrenaline is converted into adrenaline in the adrenal medulla by N-methyltransferase.

Noradrenaline is stored in the synaptic vesicles bound to ATP. On stimulation, the vesicles move towards the membrane and fuse with it. When the membrane bursts, noradrenaline is released by the process of exocytosis. After being used, the remaining noradrenaline again enters the vesicles. Noradrenaline also circulates in the blood and is taken up by other organs like the spleen. This is called extraneuronal uptake.

(ii) Acetylcholine Acetylcholine is a neurotransmitter in both the central nervous system and the peripheral nervous system. It is an ester of acetic acid and choline.

In the central nervous system, it acts as a neuromodulator and has a role in the enhancement of sensory perceptions on waking up and in prolonged attention.

In the peripheral nervous system, it activates muscles. It is an important neurotransmitter in the autonomic nervous system. It is the excitatory neurotransmitter at the neuromuscular junction. Through a sequence of events, it causes muscle contraction. It acts through a different type of receptor to inhibit contraction of cardiac-muscle fibers.

In the autonomic nervous system, it is released from the following sites:

- Pre and post-ganglionic parasympathetic nerves
- All preganglionic sympathetic nerves
- Some postganglionic sympathetic nerves—sympathetic vasodilator nerves in skeletal muscle and pseudo motor nerves to sweat glands

Acetylcholine is synthesized inside the nerve fibers. Acetyl from actylcoenzyme-A combines with choline, in the presence of the enzyme choline acetyl transferase. Maximum synthesis occurs at the nerve terminal. It is then stored in the synaptic vesicles and released on depolarization of the nerve. It acts on muscarinic receptors (found in the smooth muscles), and on nicotinic receptors (found in skeletal muscles), autonomic ganglia and some other parts of the central nervous system. It is destroyed by the enzyme cholinesterase.

(iii) Dopamine Dopamine is a catecholamine neurotransmitter. It is produced in several areas of the brain including substantia nigra, corpus striatum, neocortex, limbic system and retina. It is also a neurohormone released by the hypothalamus. Its main function is to inhibit the release of prolactin from the anterior lobe of the pituitary. It is a precursor to norepinephrine and then epinephrine in their biosynthesis pathways.

Dopamine is biosynthesized by the hydroxylation in the presence of enzyme tyrosine hydroxylase, converting the amino acid L-tyrosine to L-DOPA and then by decarboxylation of L-DOPA to dopamine. In neurons, it is stored in vesicles and released by an action potential into the synapse.

It carries out important functions like cognition and behavior, motivation, voluntary movement, sleep, inhibition of prolactin production, attention, memory and learning.

GABA Gamma amino butyric acid is the chief inhibitory neurotransmitter in the central nervous system. It is secreted in the nerve endings of cerebellum, cerebral cortex, retina and nerve endings associated with presynaptic inhibition in the spinal cord.

It binds to specific transmembrane receptors and causes opening of potassium and chloride channels. Potassium comes out of the synapse and chloride enters inside. This causes hyperpolarisation and formation of inhibitory postsynaptic potential.

Serotonin Serotonin, also known as 5-Hydroxytryptamine, is a monoamine neurotransmitter. It is derived from tryptophan. It is found in the gastrointestinal tract, hypothalamus, platelets, retina, cerebellum, limbic system, dorsal raphe of the midbrain and spinal cord. 80% of the total serotonin is located in the enterochromaffin cells of the gut, and this is important for the movements of the intestine.

It inhibits impulses of pain sensation in the spinal cord. It acts as a chemical messenger that transmits nerve signals between nerve cells. It causes vasoconstriction of blood vessels. Changes in the serotonin level in the brain can alter mood and cause depression.

(iv) Glutamate Glutamate, also known as monosodium glutamate, is the major excitatory neurotransmitter in the brain. It is involved in major brain functions such as cognition, memory and learning.

Only those cells having glutamate receptors are sensitive to glutamate. It binds to these receptor proteins. It is totally intracellular and is inactive as long as it is intracellular. Glutamate is taken up by astroglial cells and converted to glutamine. Glutamine cannot activate glutamate receptors. It enters the extracellular fluid. Nerve terminals take up this glutamine and convert it back to glutamate, which now acts. This is beneficial as it allows glutamate to be inactivated by glial cells and transported back to neurons in an inactive form.

Endorphin Endorphin is an endogenous opoid peptide neurotransmitter. It is produced by the pituitary gland and is present in the hypothalamus during exercise, excitement, orgasm, pain and consumption of spicy food.

Beta-endorphin, which is released into the blood, cannot enter the brain in large quantities because of the blood–brain barrier. Hence, the physiological effects are not very clear. The hypothalamic neurons are probably the main source. The behavioral effects of beta-endorphin are exerted by its actions in the brain and spinal cord.

2. Functional Significance of Neurotransmitters

Three criteria have to be fulfilled before one neuron can use more than one neurotransmitter. The neurotransmitter must be there in this particular neuron. The release must be under physiological conditions and both must exert their action together or separately pre or/and post-synaptic effects. Release and existence of the two or more neurotransmitters are not clearly established. But, probably, the interaction between neurotransmitters has been seen in the same neuron—substance P co-released with serotonin from bulbospinal fibers can reduce the action of the amine on specific presynaptic receptors. The functional significance of such interactions between neurotransmitters coexisting in the same neuron is very important. They could be involved in the physiological control of release of hormones from the pituitary gland.

10.3 DISORDERS OF THE BRAIN, SPINAL CORD AND PERIPHERAL NERVES

1. Dementia

Dementia is a clinical syndrome and not a specific disease. There is memory loss, inability to solve problems or control emotions. There is gradual impairment of reasoning and intellectual faculties and not being able to think well enough to carry out normal daily activities like dressing and eating. There are changes in personality and behavioral abnormalities.

There is also physical deterioration. There is decrease in food intake and emaciation. Febrile illness is poorly tolerated. Finally, there is severe confusion, stupor or coma.

Different types of dementia exist, depending on the cause. Alzheimer's disease is the most common type. Drugs cannot cure or repair the brain damage but they may slow down the disease or improve the symptoms.

Pathophysiology There is chronic, progressive, irreversible degeneration and atrophy of the cerebral cortex—cerebrum, diencephalons and possibly basal ganglia.

Sometimes there is purely thalamic degeneration.

Atherosclerotic vascular disease results in multiple foci of infarction in the cerebrum, basal ganglia, thalamus and brainstem.

Chronic increased intracranial pressure is often associated with impairment of mental function.

2. Alzheimer's Disease

Alzheimer's disease is the most common form of dementia—cortical dementia. It is a progressive, degenerative disease of the brain and is fatal. The earliest symptom is an inability to acquire new memories and loss of memory for recent events.

There is disturbance of language, agnosia, apraxia and impaired capacity for abstract thought. The person is totally incapable of caring for himself.

With advancement of the disease, there is confusion, irritability, mood swings, general withdrawal and gradually bodily functions are lost, finally resulting in death.

Pathophysiology There is degeneration and widespread loss of nerve cells in the cortical association areas, especially in the frontal, temporal and parietal lobes with secondary changes in the cerebral white matter. Cerebral convolutions are narrowed. The third and lateral ventricles are enlarged. Neuritic plaques and neurofibrillary changes are seen in the association fibers.

The exact pathogenesis is not clear but it has been found that there is marked reduction in choline acetyl esterase and acetylcholine in the hippocampus and neocortex. This is probably due to loss of the cells in basal ganglia and hence loss of cholinergic synthesis. Another observation is the decrease in amino acid transmitters—especially in glutamate—in cortical and subcortical areas.

3. Schizophrenia

Schizophrenia is the most serious unsolved disease in world society. It is a functional mental disorder of split personality, characterized by abnormality in perception or expression of reality. There is emotional withdrawal from the surroundings. There are also bizarre or paranoid delusions, auditory hallucinations and disorganized speech and thinking. There is significant social and occupational dysfunction.

There are five subtypes—paranoid, catatonic, disorganized, residual and undifferentiated types.

Pathophysiology A lot of evidence favors a genetic factor. Studies have shown that closer the relation of a person to a schizophrenic, greater the risk of having schizophrenia. If one parent is schizophrenic, chances are around 11% to 15% and if both parents are schizophrenic, chances are nearly 50% that the child will have schizophrenia. More the abnormal dopamine activity in the striatum, greater the neurocognitive defects. Zinc finger protein 804A and chromosome 6 HLA regions have been implicated.

Prenatal Theory It has been found that people with this condition are born in winter or spring. Prenatal exposure to infections increases risk for developing this condition later in life.

Current psychiatric research is focused on the role of neurobiology but, a single organic cause has not been isolated.

Intrafamily relationships have been thought to be responsible. Interpersonal relations in the family like quarrels, separation of parents and overprotection by parents interfere in some way with the normal maturation of a person. Child abuse or trauma also may play a part.

It has been postulated that neurotransmitters like norepinephrine, GABA and acetylcholine interact to maintain a balance with dopamine and hence, there is a reduction in dopaminergic transmission.

Probably a combination of all may be responsible.

4. Anxiety

Anxiety is a normal reaction to stress. It helps people cope with a situation. On becoming chronic, it becomes a disabling disorder. It is an unpleasant feeling associated with uneasiness, apprehension, fear or worry.

An anxious person feels weak, fatigued and tense and experiences headache, abdominal pain and palpitation. The body responds by increasing heart rate, rise in blood pressure and increase in blood supply to the muscles, especially the ones which need to act. There is sweating, tremors and a sense of panic and dread.

Pathophysiology No satisfactory cause is available. Hypotheses have been put forward.

Psychologists regard it as an anticipatory behavior. Some attribute it to repression of sexual urge. Anxiety is seen more in intelligent people.

Urinary excretion of epinephrine and norepinephrine is increased in these persons.

5. Depression

Depression is a state of low moods and aversion to activity. There is a feeling of sadness, helplessness, hopelessness and the person does not take interest in normal enjoyable activities. It could be slight, mild or severe.

Pathophysiology Mild depression may be related to environment. The actual cause of severe depression is not known. Exact neurotransmitters have not been detected.

The following theories have been put forward:

Genetic Theory Could be hereditary, sometimes it is in the members of the same family. Probably, there is a dominant

mode of inheritance. Locus on chromosome 6 influences the susceptibility to depressive disorders.

Biochemical Theory There is some biochemical abnormality resulting in depletion in serotonin, dopamine and norepinephrine.

Some postulate a basic fault with character development.

6. Parkinson's Disease

Parkinson's disease is a degenerative disorder of the extrapyramidal system, affecting motor skills, speech and other functions and is characterized by tremors, rigidity, bradykinesia and postural disturbances. It is a chronic progressive disorder.

The person suffering from Parkinsonism has an expressionless face, stooping posture, festinating gait and has difficulty in maintaining balance. There is slowness of movement, along with tremors and rigidity.

Parkinsonism is of the following types:

- **Primary or idiopathic**
- **Secondary**—Could be due to drugs, infections, toxic substances, vascular, degenerative
- **Inherited**—Huntington's disease, olivopontocerebellar atrophy
- Sporadic—Striatonigral degeneration

Pathophysiology It is a disorder of the extrapyramidal system affecting the basal ganglia—striatum, pallidum, substantia nigra and subthalamic nucleus.

Neurons in substantia nigra die or are impaired. There is loss of dopamine. By the time symptoms appear, there is 60 to 80% loss of dopamine-producing cells.

The balance between dopamine and acetylcholine is disturbed. Either there is increased acetylcholine or decrease in dopamine.

Another theory is that there is loss of nerve endings that produce norepinephrine, which is closely related to dopamine.

MPTP (1-methyl 4-phenyl 1,2,3,6–tetrahydropyridine) is a free radical toxin. It freely crosses the blood–brain barrier and has affinity for post-synaptic dopamine neurons of substantia nigra. It interferes with mitochondrial metabolism and results in cell death.

Lewy bodies (intracytoplasmic eosinophilic inclusion bodies) are deposits of protein alpha–synuclein along with other proteins. The exact role is not known but it is presumed that it may prevent the cell from functioning normally.

7. Infections

The blood–brain barrier acts as a very good protection to the brain and spinal cord. Yet, it could become infected by a wide spectrum of microorganisms, the most common being bacteria and virus. Rarely parasites and fungi can infect the central nervous system.

Infection can occur by the following—head injury, from infection of the middle ear, from infection elsewhere in the body infecting the CNS through blood, and sometimes by lumbar puncture (iatrogenic).

The various infections are meningitis, encephelitis, poliomyelitis, abscess and myelitis.

(a) Meningitis Meningitis is an inflammation of the meninges and the CSF. The onset is sudden and there is high fever, severe headache and neck stiffness.

Pathophysiology The most common bacteria responsible for meningitis are *Streptococcus pneumonia* causing pneumococcal meningitis, *Neisseria meningitidis* causing meningococcal meningitis and *H. influenza type b-Hib*.

When anyone is in direct contact with an infected person or directly exposed to discharges from the mouth or nose of an infected person, he/she is at risk of getting the infection. It commonly affects children. Other risk factors are chronic alcoholism, weak immune system, intravenous drug abuse, diabetes, and above 60 years of age.

(b) Encephelitis Encephelitis is an infection of the brain itself. There is headache, vomiting, fever, drowsiness and mental confusion. In severe cases, there are convulsions leading to coma and death.

Pathophysiology It can be caused by bacteria and virus. They could occur as a complication of an infection elsewhere or from adjacent meningeal infection or direct viral infection of the brain and spinal cord. Pathological changes are seen in both white and gray matter. Those who have a weak immune system are at a higher risk of getting this infection.

(c) Poliomyelitis Poliomyelitis is an acute viral infection. There is mild fever, weakness and malaise and in mild cases there is recovery but if infection is serious, it could lead to paralysis of the affected part. Rarely, respiratory complication can end in death.

Pathophysiology The infection is caused by a virus called poliovirus and sometimes by other enteroviruses. It spreads by fecal-oral route—food contaminated by infected fecal matter.

The virus enters through the mouth and infects the cells of the throat and the intestinal mucosa. It binds to the receptor on the cell membrane and begins to multiply. It divides within the gastrointestinal cells for a week and then spreads to the tonsils, the intestinal lymphoid tissue affecting the Peyer's patches and to the cervical and mesenteric lymph nodes, where they further multiply. The virus then enters the blood and spreads throughout the body.

(d) Myelitis It is an inflammatory lesion of the spinal cord disrupting central nervous system functions, linking the brain with the limbs, either infective or non-infective. The onset is acute or subacute and symptoms vary depending on the region affected. There is fever, pain in the back, maximally in the thoracic region, sensory loss below the level of lesion, partial or complete paralysis and retention of urine.

Pathophysiology It follows a viral infection (poliomyelitis, herpes zoster, herpes simplex, enterovirus) or a bacterial infection (pyogenic cord, meningovascular syphilis, and tuberculosis). Viral infection is more common. Parasitic and fungal infections less commonly cause myelitis.

There is destruction of neurons, meninges and white matter alone or in combination. The cord is edematous, hyperemic and infiltrated with inflammatory cells. Nerve-cell destruction may be selective. The herpes zoster virus affects dorsal root ganglia while the poliomyelitis virus affects anterior horn cells.

Axis cylinder and myelin sheath are destroyed. In severe cases, the cord may get softened.

8. Peripheral Neuropathy

Peripheral neuropathy is a condition where there is damage to the nerves of the peripheral nervous system, which could result either from disease of the nerve itself or from side effects of some systemic illness.

The lesions may involve one or more nerves, it could be acute or chronic, it could affect the nerves multipally but unequally, and it could involve the autonomic part of peripheral nerves. Hence there are four patterns of peripheral neuropathy—polyneuropathy, mononeuropathy, mononeuritis multiplex and autonomic neuropathy. The most common of these is peripheral polyneuropathy affecting mainly the feet, legs and later on the hands.

It can be classified also on the type of nerves affected—motor, sensory, mixed and autonomic or depending on the cause, e.g., hereditary, acquired (inflammatory).

Pathophysiology

The various conditions causing peripheral neuropathy are metabolic (diabetes), toxins (vincristine), genetic diseases (Friedreich's ataxia), inflammation (Guillain–Barre syndrome), vitamin deficiency (B12), malignancy, radiation and chemotherapy.

Frequently, the cause may not be identified and it is called idiopathic.

Demyelination of the spinal roots and/or peripheral nerves is the pathology.

9. Cerebrovascular Disease

Cerebrovascular disease is the third commonest cause of death in developing countries. It includes all disorders in which an area of the brain, transiently or permanently, is affected by ischemia or block or bleeding. The dysfunction is related to disease of the blood vessels supplying the brain. It is a medical emergency and requires immediate treatment.

Symptoms are in the form of headache, vomiting, convulsions, confusion, disorientation. Sometimes it manifests as sudden severe headache and collapse of the person and sometimes even sudden death from a massive bleed. Hemiplegia (paralysis) of the opposite side is common.

Pathophysiology There could be spasm of one of the cerebral vessels. It can result from embolism or rupture of a blood vessel. Spontaneous rupture of an aneurysm causes a hemorrhagic stroke. The walls of the aneurysm get weak and even with a minimum rise of blood pressure; there can be tear or rupture leading to bleeding into the brain tissue. This is seen with weak arteries having atheromatous deposition. When this bleeds there is a hemorrhagic stroke in the form of cerebral hemorrhage, subarachnoid hemorrhage or both.

Deprivation of blood supply leads to infarction of the cerebral tissue within a few minutes. Amino acids are released which promote calcium influx and exacerbate the neural damage. The damaged neurons and glia become edematous, resulting in cerebral edema. There is further damage to brain tissue due to impaired blood flow.

REVIEW QUESTIONS

1. Write a note on nervous tissue with a diagram.
2. Enumerate the cranial nerves. Write on the 5th and 7th cranial nerves.
3. Describe the formation of the spinal nerve. Describe in detail the brachial plexus.
4. Name the various parts of the brain with their functions.
5. Describe the structure of the cerebrum.
6. Describe internal and external structure of the spinal cord with a diagram.
7. Discuss the structure, functions and disorders of the cerebellum.
8. Describe the autonomic nervous system. Differentiate between sympathetic and parasympathetic system.
9. Describe the structure of a neuron with a labeled diagram. Explain action potential.
10. Describe electrical transmission in a nerve fiber.
11. Describe the structure of a neuromuscular junction. How is an impulse transmitted from nerve to muscle?

12. Define and classify synapse. What is its function?
13. Explain reflex action. Classify different types of reflex action.
14. What are receptors? Classify them. Give their properties.
15. Which are the various stages of sleep? Describe them.
16. What are neurotransmitters? Classify them and describe them.
17. Briefly discuss the disorders of the nervous system with emphasis on pathophysiology.
18. Write short notes on:
    a. Hypothalamus
    b. Limbic system
    c. Extrapyramidal system
    d. Brain stem
    e. Reticular formation
    f. Meninges
    g. CSF
    h. Ventricles of the brain
    i. Blood brain barrier
    j. Sensations
    k. EEG
    l. Speech
    m. Neurons
    n. Sympathetic nervous system
    o. Parasympathetic nervous system
    p. Action potentials
    q. Acetylcholine
    r. Adrenaline
    s. Noradrenaline
    t. Dopamine
    u. Parkinsonism
    v. Brain infections
    w. Anxiety and depression

Chapter

11 Special Senses

- **EYE**
  - **Anatomy**
    - **Outer structure of the eye**
      - **Sclera**
      - **Cornea**
      - **Choroid**
      - **Ciliary body**
      - **Iris**
      - **Lens**
      - **Retina**
    - **Interior of the eye**
    - **Optic nerve**
      - **Lesions in the optic nerve**
      - **Defects**
  - **Physiology of vision**
    - **Constriction of pupils**
    - **Convergence of eyeballs**
    - **Changing the power of the lens**
  - **Disorders**
    - **Errors of refraction**
      - **Myopia, Hypermetropia,**
      - **Astigmatism, Presbyopia**
    - **Glaucoma**
    - **Cataract**
    - **Detachment of retina**
    - **Conjunctivitis**
    - **Trachoma**
    - **Chalazion**
    - **Stye**
    - **Night blindness**
    - **Color blindness**
- **EAR**
  - **Anatomy**
    - **External ear**
      - **Auricle**
      - **Blood supply**
      - **Lymphatic drainage**
      - **Nerve supply**

- External acoustic meatus
  - Blood supply
  - Lymphatic drainage
  - Nerve supply
  - Applied anatomy
- Tympanic membrane
  - Applied anatomy
- Middle ear
  - Contents
  - Boundries
  - Functions
    - Arterial supply
    - Venous drainage
    - Nerve supply
  - Applied anatomy

○ **Ear ossicles**
- Malleus
- Incus
- Stapes

○ **Inner ear**
- Bony labyrinth
  - Vestibule, Cochlea
  - Semicircular canals
- Membranous labyrinth
  - Saccules and utricles
  - Spiral duct

○ **Physiology of hearing**
- Types of conduction
- Hearing defects
- Methods of examination
  - Rinne's test
  - Weber's test
  - Audiometry

○ **Physiology of balance**

○ **Disorders**
- Meniere's disease
- Acoustic neuroma
- Hearing loss
- Otitis media
- Labyrinthitis
- Otosclerosis

- **PHYSIOLOGY OF SMELL**
- **PHYSIOLOGY OF TASTE**

Introduction

Senses of hearing, sight, smell and taste, all have specialized sensory receptors.

These organs are:

- Vision–Sight – Eyes
- Hearing – Ears
- Smell – Nose
- Taste – Tongue

Thus eyes, ears, nose and tongue are the organs which are called special organs for senses.

11.1 EYE

Eyes are the organs of sight that detect light and send signals along the optic nerve (2nd cranial nerve) to the visual area of the brain.

11.1.1 Anatomy

The eye captures and analyzes light. It has a lens to focus the light that enters it and cells to process the light. It is spherical in shape and has a diameter of about 2.5 cm. The space between the eye and the orbital cavity is occupied by adipose (fat) tissue. The eye is protected from injury by the bony wall and the fat. Structurally, the two eyes are separate but their activities are coordinated so that they function as a pair.

It is possible to see with only one eye but the three-dimensional vision is impaired when only one eye is used.

1. Outer Structure of the Eye

Inside the eyeball are the lens, aqueous humor and vitreous humor.

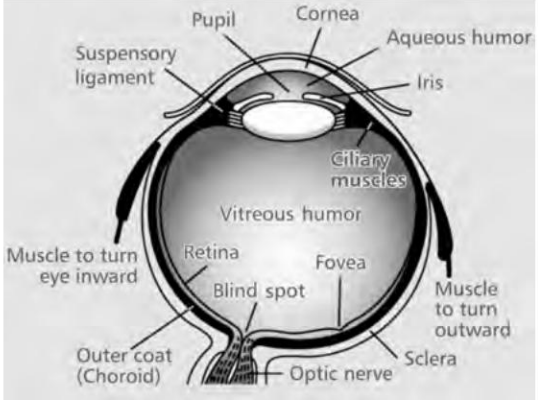


Fig. 11.1 *Outer structure of eye*

There are three layers of tissue in the walls of the eye.

- Outer fibrous layer—sclera and cornea
- Middle vascular layer or uveal tract—choroids; ciliary body and iris
- Inner nervous tissue layer—retina

(a) Sclera The sclera is an opaque, fibrous, protective outer structure found on the lateral and posterior aspects of the eye. It is firm and is composed of dense fibrous tissue. Many optic nerve fibers perforate the sclera posteriorly giving it a sievelike appearance and hence it is also called the **lamina cribrosa**. It is pierced by the optic nerve, choroid veins, ciliary nerves and anterior ciliary arteries. The sclera is fused posteriorly with the dural sheath of the optic nerve.

The outer surface of the sclera is white and smooth and the inner surface is brown in color as it is grooved by ciliary nerves and vessels.

Anteriorly, the sclera is covered by the conjunctiva—a thin, transparent membrane that is involved in protection of the eyes. The conjunctiva also lines the insides of the eyelids.

The sclera is continuous anteriorly with the cornea at the sclerocorneal junction, known as **limbus**. The deep part of the limbus contains a circular canal called **canal of Schlemn**, and the aqueous humor drains into the anterior veins through this sinus. The sclera maintains the shape of the eye and gives attachment to the eye muscles.

(b) Cornea Anteriorly, the sclera continues as the cornea. It is a transparent, dome-shaped structure at the front of the eye. It is more convex than the sclera, but curvature diminishes with age. It maintains the shape of the eyeball. It protects the inner structures and together with the lens helps focus and direct light onto the retina.

It is separated from the iris by a space called the anterior chamber of the eye.

Structurally, the cornea consists of the following layers from front to back:

- Corneal epithelium
- Bowman's membrane (anterior elastic lamina)
- Substantia propria
- Descemet's membrane (posterior elastic lamina).

(c) Choroid It is a thin pigmented layer which separates the posterior part of the sclera from the retina.

Anteriorly, it merges with the ciliary body and posteriorly it is perforated by the optic nerve. It is very rich in blood vessels and is deep chocolate brown in color. This network of blood vessels supplies nutrients to the cells and removes waste products.

Structurally, it consists of

- Outer vascular lamina
- Middle capillary lamina
- Inner basal lamina

As it is pigmented, it makes the retina appear black, thus preventing reflection of light within the eyeball and also prevents scattering of light.

(d) Ciliary Body The ciliary body is the anterior continuation of the choroid, consisting of ciliary muscles and secretory epithelial cells. It suspends the lens and helps it in accommodation for near vision. It gives attachment to the suspensory ligament, which, at its other end is attached to the capsule, enclosing the lens. Contraction and relaxation of the ciliary muscle changes the thickness of the lens which bends or refracts light rays entering the eye to focus them on the retina.

Epithelial cells secrete aqueous fluid into the anterior segment of the eye, i.e., the space between the lens and cornea.

The ciliary muscle is a ring of unstriped muscles and is of two types—radial and circular.

Radial fibers radiate backwards and relax the suspensory ligament of the lens so that the lens becomes more convex for near vision.

Circular fibers, on contraction, relax the suspensory ligament and the lens becomes more convex; so there is accommodation of the eye.

(e) Iris The iris is the anterior part of the uveal tract. It is the visible colored part of the eye and extends anteriorly from the ciliary body, lying behind the cornea and in front of the lens. It divides the anterior segment into anterior and posterior chambers.

It is a pigmented muscular structure consisting of an inner ring of circular muscle and an outer layer of radial muscle. The color of the iris is genetically determined and depends on the number of pigment cells present. If pigment cells are absent, the iris is blue in color due to diffusion of light in front of the black posterior surface.

In the centre of iris there is an opening called the **pupil** from where light is allowed to pass. In bright light it is constricted, and in dim light it is dilated. Contraction of circular muscle fibers constricts the pupil and contraction of radial fibers dilates it.

The iris is supplied by parasympathetic and sympathetic nerves. Parasympathetic stimulation constricts the pupil and sympathetic stimulation dilates it.

Its function is to help control the amount of light entering the eye so that too much light does not enter the eye and damage the retina and enough light enters to allow a person see properly.

(f) Lens The lens is a transparent, flexible, bi-convex structure, placed between the anterior and posterior segments of the eye. It is highly elastic and lies immediately behind the pupil. It is circular in outline and has a diameter of 1 cm.

The central points of the anterior and posterior margins are called the **poles**. The line connecting the poles forms the axis of the lens.

It is suspended from the ciliary body by the suspensory ligament and this ligament controls its thickness. The lens is enclosed in a capsule. The centre of the lens is firm, while the periphery is soft.

The lens bends the light rays reflected by objects in front of the eye using its refractive properties.

It is the only structure in the eye that can vary its refractory power which is achieved by changing its thickness. When the ciliary muscle contracts, it moves the suspensory ligament forward, releasing its pull on the lens thus, increasing its thickness, and helps in focusing a clear image on the retina for both near and distant objects by changing its convexity. The nearer the object being viewed, the thicker the lens becomes to allow focusing.

(g) Retina The retina is a thin, transparent, complex, delicate structure which forms the innermost layer of the eye. It is multilayered and has many neurons and synapses. The only neurons that are directly sensitive to light are the photoreceptor cells—rods and cones.

Neural signals from the **rods** and **cones** undergo complex processing by other neurons of the retina. The output takes the form of action potentials in retinal ganglion cells whose axons form the nerve. There are relay neurons and sensory neurons that pass impulses along the optic nerve to the part of the brain that controls vision.

The axons of the ganglion cells form the optic nerve. Opposite to the entrance of the optic nerve there is a circular area called the **optic disk**. The depressed area of the optic disk is called the **physiological cup**. The physiological cup lacks photoreceptors and is insensitive to light and hence is also called the **physiological blind spot**.

The retina lines about three quarters of the eyeball and is thickest at the back of the eye and thins out anteriorly, and ends just behind the ciliary body. Near the centre of the posterior part of the retina is the yellow spot—**macula lutea**. In the center of this area is a little depression consisting of only cone-shaped cells, called the **fovea centralis**. Anteriorly, the retina has fewer cones than rod-shaped cells.

About 0.5 cm to the nasal side of the yellow spot or macula lutea, the nerve fibers of the retina converge to form the optic nerve.

The retina is composed of the following ten layers:

1. Outer pigmented layer
2. Layer of rods and cones
3. External limiting membrane
4. Outer nuclear layer
5. Outer molecular layer
6. Inner nuclear layer

7. Inner molecular layer
8. Ganglion cell layer
9. Nerve fiber layer
10. Internal limiting membrane

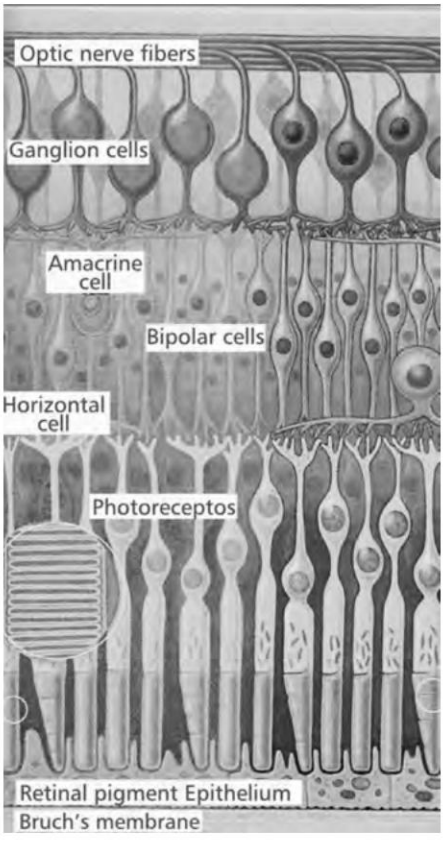


Fig. 11.2 *Principal neurons of the retina*

The outer pigment layer contains the pigment **melanin**. After this layer are the two types of photoreceptor cells, the rods and cones, which contain photosensitive pigments. There are approximately 120 million rods and 6 million cones. Rods are elongated—40–60 uv in length and 2 u in diameter. Cones are pyramidal in shape—28–82 uv in length and 2.5 u in diameter. 10 to 12 rods connect to one nerve cell, whereas one cone is connected with its own nerve cell. Rods function mainly in dim light, while cones support daytime vision. A third, much rarer type of photoreceptor, the photosensitive ganglion cell, is important for reflexive responses to bright daylight.

Besides the rods and cones there are other neurons which synapse with one another. They are the horizontal cells, the bipolar cells, amacrine cells and ganglion cells.

Rods and cones convert light rays into nerve impulses which are conducted to the occipital lobe of the cerebrum via the optic nerve.

Rods contain the light sensitive pigment **rhodopsin** and cones contain **iodopsin**. Rhodopsin contains the protein **scotopsin** and the carotenoid pigment **retinal**. Iodopsin contains the protein **photopsin**.

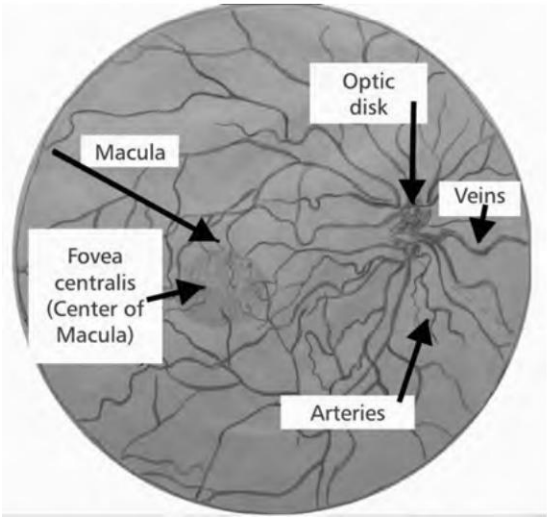
Arterial Supply

- Ciliary arteries
- Central retinal artery

Venous Drainage

- Central retinal vein

Central retinal vein and artery are encased in the optic nerve entering the eye at the optic disk



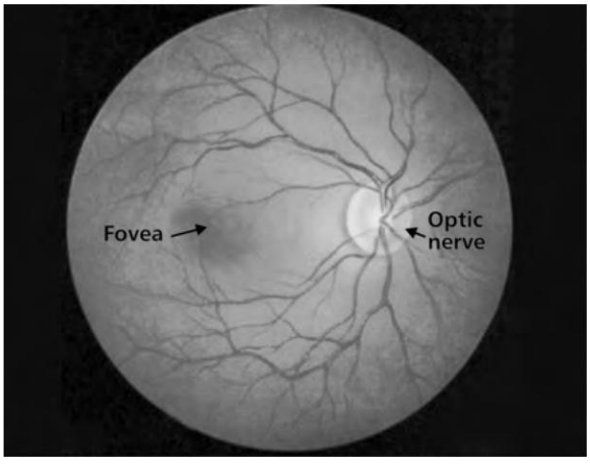


Fig. 11.3 *Human retina*

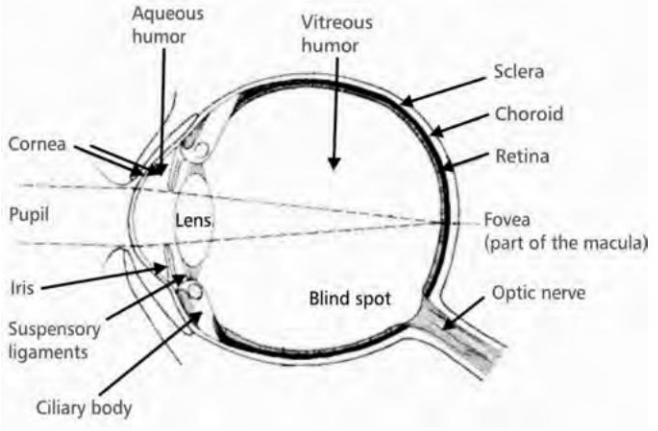


Fig. 11.4 *Interior of the eye*

2. Interior of the Eye

The interior of the eye is divided by the lens into a smaller anterior segment and a bigger posterior segment.

The anterior segment of the eye is divided into anterior and posterior chambers by the iris. The anterior chamber is filled with a watery fluid, the **aqueous humor**, or aqueous. Produced by secretory cells of the ciliary body, the aqueous humor passes first into the posterior chamber (between the lens and iris) and then flows forward through the pupil into the anterior chamber of the eye. Then it returns to the venous circulation through the venous sinus in the angle between the iris and cornea. This is important because it is the site where the aqueous humor drains out of the eye. If the aqueous humor cannot properly drain out of the eye, pressure can build up inside the eye, causing optic-nerve damage and eventually loss of vision, a condition known as glaucoma.

The aqueous humor supplies nourishment to the eye and surrounding tissues and removes waste from these structures.

The **vitreous humor** is a clear, soft, colorless transparent gel which occupies the posterior compartment of the eye, located between the crystalline lens and the retina and occupying about 80% of the volume of the eyeball to hold its spherical shape. Light initially entering the eye through the cornea, pupil and lens, is transmitted through the vitreous to the retina.

The vitreous humor consists of 99% water, and a small amount of collagen fibrils, peripheral cells, sugar, and ascorbic acid.

It supports the retina against the choroid and prevents the walls of the eyeball from collapsing.

3. Optic Nerve

The optic nerve is a continuation of the axons of the ganglion cells in the retina. There are approximately 1.1 million nerve cells in each optic nerve. The fibers converge to the nasal side of macula lutea. The nerve leaves the back of the orbit through the optic foramen. It goes backwards and medially to

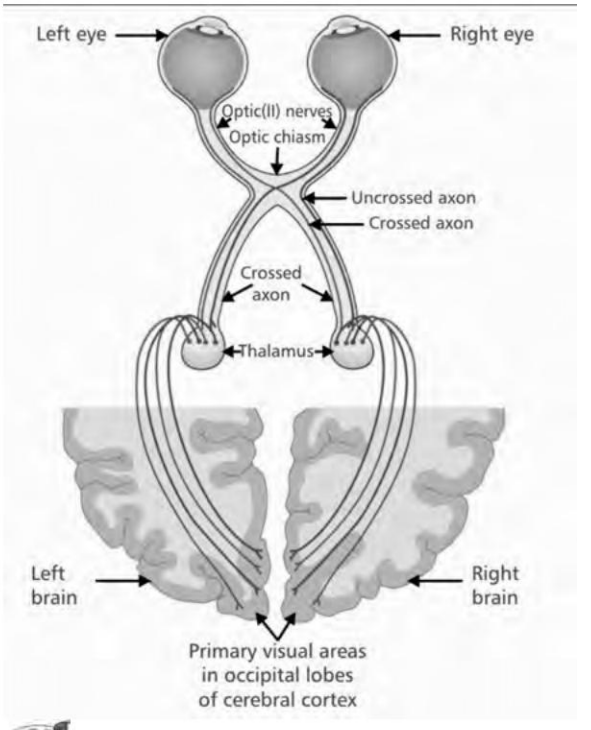


Fig. 11.5 *Optic nerve (Refer colour figure)*

meet the nerve from the other eye in front of and above the pituitary gland at the optic chiasma. In the optic chiasma, the optic nerve fibers emanating from the nasal half of each retina crosses over to the other side; but the nerve fibers originating in the temporal retina do not cross over but continue backwards on the same side as the optic tract.

The nerve fibers of the optic tract have nasal fibers from the retina of one eye and temporal fibers from the retina of the other. The optic tract passes backwards to synapse with nerve cells of the lateral geniculate body of the thalamus. Then, nerve fibers go backwards and medially as the optic radiation and end in the visual area of the cerebral cortex, which is in the occipital lobe of the cerebrum. The visual cortex ultimately interprets the electrical signals produced by light stimulation of the retina, via the optic nerve, as visual images. Some fibers from the lateral geniculate body go to the cerebellum and with impulses from semicircular canals of the ears, from the skeletal muscles and joints contribute to the maintenance of posture and balance.

(a) Effect of Lesions in the Optic Nerve at Various Levels The optic pathway includes the retina, the optic nerve, the optic chiasm, the optic radiations and the occipital cortex. Damage along the optic pathway causes a variety of visual field changes.

Loss of vision in one field is called **anopia**.

Loss of vision in one half of visual field is called **hemianopia** which is of two types—**homonymous hemianopia**, where there is loss of vision in the same halves of both the

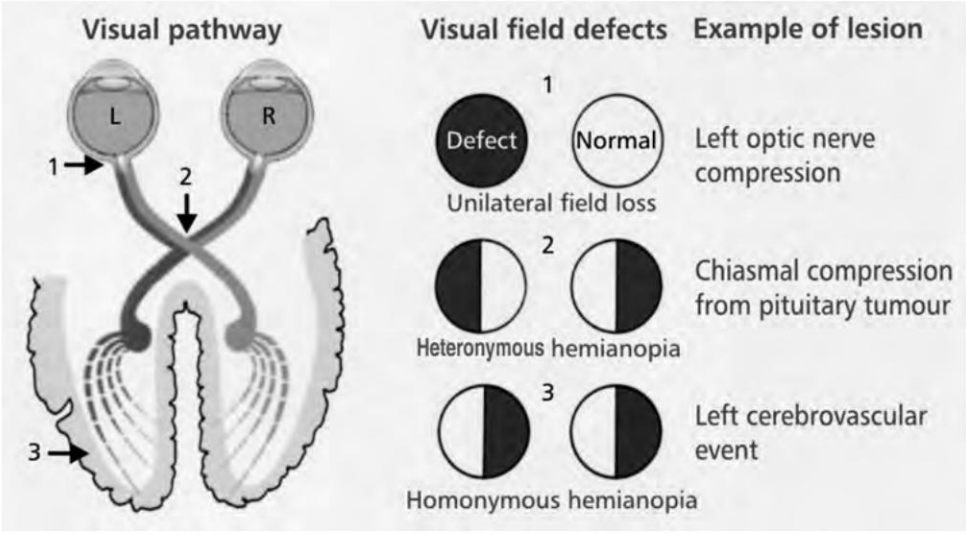


Fig. 11.6 *Defects of the optic nerve*

visual fields, **heteronymous hemianopia** where the loss is in opposite halves of visual fields.

(b) Defects Prechiasma lesions cause field defects in the ipsilateral (same side) eye only (so if a lesion is in the left optic nerve, field defect occurs in the left eye only and right visual field will remain unaffected). (See Fig. 11.6)

Optic nerve lesion will cause total blindness on the same side.

In optic chiasma with central lesions, the defect will be bitemporal hemianopia. With lateral lesions, it will be right or left hemianopia corresponding to the side.

Optic-tract lesions cause homonymous hemianopia. The same lesion is seen in lateral geniculate body and optic radiation lesions. With damage on one side, the visual fields will be absent on the opposite side in both eyes—homonymous hemianopia.

A lesion affecting both visual lobes will be devastating to vision and result in cortical blindness.

11.1.2 Physiology of Vision

Light waves travel at a speed of 186,000 miles per second. Light is reflected into the eyes by objects within the field of vision.

As a light wave passes from the air into the eye, it moves sequentially through the cornea, aqueous humor, pupils, lens and vitreous humor. Then it passes through the neural layer of the retina to the photoreceptors behind.

Within the layers of the retina, light impulses are changed into electrical signals by rods and cones of the retina through some chemical reactions.

These electrical signals are sent through the optic nerve, along the visual pathway, to the occipital cortex, where the electrical signals are interpreted by the brain as a visual image. Thus, the process of visual sensation may be explained on the basis of image formation along with neural, chemical and electrical phenomena. Processes involved in producing a clear image are refraction of light rays, changing the size of the pupils and accommodation of the eyes.

Light rays entering the eye need to be refracted to focus them on the retina.

The lens bulges forward increasing its convexity and focuses light rays from near objects on the retina. This change in convexity and curvature of the lens is called **accommodation.** Light from distant objects needs least refraction and as the object comes nearer, amount of refraction needs to be increased. For near objects, the ciliary muscle contracts pulling on the suspensory ligament leading to shortening, thickening and bulging of the lens, thus increasing the curvature.

The image falling on the retina is an inverted one and reversed side to side. Still, the object which is seen is upright, i.e., as the object is in the field of vision. This is due to the role played by the cerebral cortex.

Pupil size influences accommodation by controlling the amount of light entering the eye. In bright light, pupils are constricted, and in dim light, they are dilated.

If pupils dilate in bright light, too much light would enter the eye and that can damage the sensitive retina. If in dim light, pupils constrict, insufficient light would enter the eye to activate the photosensitive pigments in the rods and cones which stimulate the nerve endings in the retina and the image formed would not be clear.

Contraction of circular fibers of the iris constricts the pupil and contraction of radiating fibers dilates it.

For objects which are near, the eye makes the following adjustments:

1. Constriction of Pupils

Constriction of pupils helps in accommodation by reducing the width of the light beam.

2. Convergence of Eyeballs

Light rays from near objects enter the two eyes at different angles and stimulate corresponding areas of the two retinas. Both the eyeballs move in such a way that they are directed towards the object.

Extraocular muscles move the eyes and rotate the eyes so that they converge on the object seen. Nearer the object, greater the eye rotation needed for convergence. If convergence is not achieved, then eyes focus the image on different parts of the retina and two images are sent to the brain leading to **diplopia**—double vision.

3. Changing the Power of the Lens

Thickness of the lens changes to focus light on the retina. Adjustment depends on the distance of the object from the eyes. The lens is thicker for near vision and is thinnest for objects more than 6 meters distance.

For distant vision, objects more than 6 meters away from the eyes are focused on the retina without adjustment of the lens or convergence of the eyes.

Thus, light rays from objects stimulate the retina leading to a sequence of potential changes. The formation of image on the retina is converted into a nerve impulse. Rhodopsin and/or iodopsin are activated. Hyperpolarisation results and impulses that are formed are conveyed via the optic nerve to the cerebral cortex and vision is perceived.

11.1.3 Disorders

1. Errors of Refraction

An eye that has no refractive error when viewing a distant object, is said to have **emmetropia** or is said to be emmetropic. An eye that has a refractive error when viewing a distant object is said to have **ametropia** or is said to be ametropic.

In the emmetropic eye, light rays entering the eye are focused on the retina by the cornea and the lens, creating a sharp image that is transmitted to the brain. During accommodation, the ciliary muscles adjust the shape of the lens to properly focus images. Refractive errors are failure of the eye to focus images sharply on the retina, causing blurred vision.

The following are the types of refractory errors:

(a) Myopia In myopia, or nearsightedness, the point of focus is in front of the retina or the axial length of the eye is too long, or both. Distant objects are blurred, but near objects can be seen clearly. The eyeball is longer than normal and the parallel rays are not focused on the retina but in front of the retina. To correct myopia, a bi-concave (minus) lens is used.

(b) Hypermetropia In hypermetropia, or farsightedness, the point of focus is behind the retina or the axial length is too short, or both. The lens may also remain less convex. Near objects are blurred. Distant objects are focused normally. To correct hypermetropia, a convex (plus) lens is used.

(c) Astigmatism In astigmatism, abnormal curvature of the cornea or lens causes light rays of different orientations (e.g., vertical, oblique, horizontal) to focus at different points, and prevents focusing on the retina. The rays of one plane (vertical) and another (horizontal) do not come to a common point of focus on the retina. To correct astigmatism, a cylindrical lens (a segment cut from a cylinder) is used.

(d) Presbyopia In presbyopia, there is loss of the lens' ability to change shape to focus on near objects due to aging. It starts usually after the age of 40. A convex (plus) lens is used for correction when viewing near objects.

2. Glaucoma

Glaucoma is a disease in which the optic nerve is damaged, leading to progressive loss of vision. The nerve damage involves loss of retinal ganglion cells. It is often, but not always, associated with increased pressure of the fluid of the eye.

Glaucoma is of two types—**open-angle** and **closed angle glaucoma**. Closed-angle glaucoma appears suddenly and is usually painful; loss of vision progresses quickly. Early diagnosis and treatment are most important in preventing loss of vision. Open-angle is chronic glaucoma which progresses at a slower rate and the patient may not notice that they have lost vision until the disease has progressed significantly.

Pathophysiology Intraocular pressure is maintained by production of aqueous humor and its drainage through the venous sinus or canal of Schlemn. Glaucoma occurs due a disturbance or imbalance between the production and drainage of the aqueous humor, thus causing increased intraocular pressure. In open-angle glaucoma, there is reduced flow through the canal and in closed-angle glaucoma, the iris is pushed forward against the canal wall, thus blocking fluid from escaping.

Many hypotheses have been put forward due to the inconsistent relationship of glaucomatous optic neuropathy with ocular hypertension. They have postulated immune mechanism, trauma, retinal-ganglion-cell degeneration and defective eye development.

Precipitating factors like tea, coffee, caffeine products, decrease in fluid intake and lifting heavy weights should be avoided by patients of glaucoma as this could increase intraocular pressure.

3. Cataract

Cataract is a change in the clarity of the lens and results in its opacity. It is a gradual process of aging but occasionally could

occur rapidly. It usually affects both the eyes but almost one eye is affected earlier than the other.

Cataracts may be partial or complete, stationary or progressive, hard or soft. It can also be named according to location—anterior (common senile cataract) and posterior (due to steroid use).

Pathophysiology Cataract is generally due to degenerative changes in old age. It can develop due to long-term exposure to ultraviolet light, exposure to radiation, microwave radiation and infrared radiation, secondary effects of diseases like diabetes, hypertension, or due to trauma. Some drugs such as steroids can induce cataract development.

The lens is made mostly of water and protein. Specific proteins are responsible for maintaining its clarity. Over the years, the structure of the lens proteins gets altered. There is denaturation of proteins ultimately leading to clouding of the lens. Genetic factors are often a cause of congenital cataracts, and family history may also play a role in predisposing to early cataract. Cataracts can also be produced by eye injury. Allergic or atopic conditions can also quicken the progression of cataracts, especially in children. Iodine deficiency can also produce cataract.

4. Detachment of Retina

Retinal detachment is a disorder of the retina in which the retina detaches itself from the underlying layer of the eye. Initially, the detachment could be localized, but if rapid treatment is not given, the entire retina could get detached. The pigmented layer gets separated from the nerve layer and deprives it of blood supply. There is loss of vision and blindness.

Pathophysiology Retinal detachment can occur following an injury to the eye or sometimes after head injury or face injury. There is a tear in the retina, which allows vitreous fluid to seep through the retina, peeling it away.

Persons with high levels of nearsightedness have longer eyeballs with thinner retinas and hence are more prone to detachment.

Cataract surgery, tumors, eye diseases, systemic diseases such as diabetes and sickle cell disease may also cause retinal detachments.

Sometimes sudden fluid movements in the eye detach the retina.

5. Conjunctivitis

Conjunctivitis, also called **pink eye**, is an inflammation or infection of the conjunctiva. It may affect one or both eyes. It is common in children. Some forms can be highly contagious and easily spread in schools and homes.

Pathophysiology Conjunctivitis can be caused by a viral or bacterial infection. It can also occur as a part of allergic reaction to irritants in the air like smoke and pollen and irritants like shampoos. It can also occur due to some ingredients in cosmetics or due to chlorine in water, especially in swimming pools. Occasionally, it can occur due to gonorrhea and Chlamydia, but is less common. Sometimes it can occur in contact-lens wearers due to allergy.

6. Trachoma

Trachoma is an infectious eye condition, or a chronic conjunctivitis. There is follicular sub-conjunctival hyperplasia.

Pathophysiology Trachoma is caused by *Chlamydia* **tracomatis**. It is spread by direct contact with eye, nose and throat secretions from affected persons. It can also spread by contact with objects like towels or handkerchiefs having infected secretions. Flies can be a route of transmission.

Children are more susceptible. It is common in areas with poor personal hygiene, poor localities and crowded places and in schools.

7. Chalazion

Chalazion is a cyst or lump in the eyelid caused by inflammation of a blocked meibomian gland, usually on the upper eyelid. Occasionally, it could become red, warm and painful.

A stye is also a lump in the eyelid caused by obstruction of an oil gland but a chalazion is not a stye. A stye represents an infection while a chalazion is an inflammation.

Pathophysiology The narrow opening, through which a meibomian gland secretes its material, gets blocked due to hardening of the sebaceous liquid near its opening. There is accumulation of the material and the gland swells. This is followed by thickening of the walls of the gland and oil leaks into the eyelid. This leads to inflammation of the gland and the eyelid.

8. Stye

A stye is a swelling on the eyelid, usually caused by an infection. It can appear on the outside of the eyelid (external stye) or on its undersurface (internal stye).

External stye is also called **hordeolum**. They can be seen as small red lumps. Internal stye causes a red bump underneath the lid with generalized redness and swelling visible on the outside.

Pathophysiology The most common cause of stye is a staphylococcal (staphylococcus aureus) infection. It can also occur due to blocking of an oil gland. External stye is more common and is due to an infection of the sebaceous glands of Zeis, at the base of the eyelashes. It can also occur due to an infection of the apocrine sweat glands of Moll. Internal stye is the result of an inflammation in one of the meibomian glands in the eyelid. It could occur either due to infection or blockage.

Styes are seen at all ages but are more common in children. It is triggered by lack of hygiene, poor nutrition, rubbing of the eyes and deprivation of sleep.

Styes are commonly associated with blepharitis. It is a chronic inflammation of the edge of the eyelid and can affect the inside or outside of the eyelids.

9. Night Blindness

Night blindness is the inability to see properly at night or in dim light. It is a symptom of an underlying disorder and not a disease by itself.

Pathophysiology Night blindness is due to a disorder of the cells of the retina that are responsible for vision in dim light.

The causes can be categorized as genetic or acquired, stationary or progressive. Common causes include retinitis pigmentosa, vitamin A deficiency, myopia, cataract or certain medicines.

Retinitis pigmentosa is the most common genetic cause of night blindness.

Vitamin A deficiency is the most common acquired cause. Vitamin A is an important nutrient for the nerve cells of the retina. It is needed in considerable amount for light detection. It is a component of rhodopsin and switches between the "on" and "off" positions in the presence of light. Vitamin A is necessary to turn rhodopsin from on to off configuration. Hence, in its deficiency, the function of the rod cells deteriorates, and leads to night blindness.

10. Color Blindness

Color blindness is the inability to distinguish different colors of the spectrum that can be distinguished by others. The difficulties can range from mild to severe. It is actually a misleading term because people with color blindness are not actually blind. Rarely, some are completely color blind and can see only in black and white.

Pathophysiology Color blindness is most often of genetic nature, but may occur due to eye, brain or nerve damage or due to exposure to certain chemicals.

Cones are responsible for color vision. There are three types of cones—red, blue and green—which enable people to see a wide spectrum of colors. An abnormality of any of the types of cones will lead to abnormal color vision.

There are three basic variants of which red/green color blindness is the most common deficiency. Red/green and blue color blindness is located on two different gene locations.

Acquired color blindness is usually due to chronic illnesses like diabetes mellitus, liver disease, glaucoma, Alzheimer's disease, Parkinson's disease, macular degeneration and sickle-cell anemia. Some medicines like antibiotics, barbiturates, drugs used to treat high blood pressure, tuberculosis and nervous disorders can cause color blindness.

11.1.4 Examination or Tests for Vision

(a) Acuity of Vision Finger counting is done with one, two and three fingers at different distances one by one. Each eye is tested separately. If finger counting appears affected, then a beam of light is thrown on the eye and patient is asked if he is able to perceive it. If finger counting is normal then the patient is asked to read from a book and tested for near vision. For distant vision, a Snellen's chart is used.

(b) Field of Vision Confrontation method is done whereby the patient's field of vision is compared with the examiners. The distance between them is one meter. All the four quadrants are tested and the examiner compares his field of vision with that of the patient. Each eye is tested separately.

For a detailed analysis of the visual field, perimetry is required in which visual fields are tested and plotted.

(c) Color Vision Each eye is tested separately and various familiar colors are shown to the patient for identification. Color blindness is usually congenital and red–green color blindness is more frequently seen.

(d) Fundus Examination This is done with the help of an ophthalmoscope. In this test, the optic disk, retinal arteries and veins are seen and it is also seen if there are exudates or hemorrhages.

11.2 EAR

The ear is the sense organ of hearing. It is supplied by the 8th cranial nerve. It not only acts as a receiver for sound, but plays a major role in maintaining the equilibrium of the body and the body position. The ear is a part of the auditory system.

11.2.1 Anatomy

With the exception of the pinna which is called the **auricle**, the other structures are encased within the petrous portion of the temporal bone.

The ear consists of three parts—the external ear, the middle ear and the internal ear. (See Fig. 11.7)

Sound can be heard and processed if all these parts work together.

1. External Ear

The external ear consists of the pinna, concha and the external acoustic meatus. They gather sound energy and focus it on the eardrum.

(a) The Auricle (Pinna) The auricle is the visible expanded portion seen on the lateral side of the head. Its function is to collect and focus sound waves. It is covered with skin and is

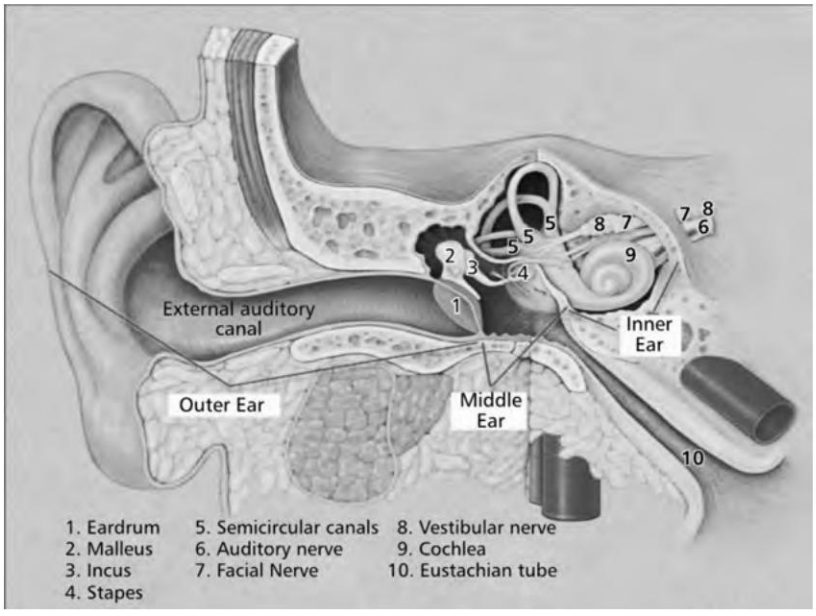


Fig. 11.7 *Anatomy of the ear*

composed of a thin plate of yellow, fibro-elastic cartilage. It is connected to the beginning of the external acoustic meatus by fibrous tissue. It is deeply grooved and ridged and the most prominent outer ridge is called the **helix**.

The lowest part of the helix is called the **lobule**. It is soft and consists only of connective tissue covered by skin. There is a large depression called the **concha** which leads into the external acoustic meatus.

Blood Supply Posterior auricular and superficial temporal arteries.

Lymphatic Drainage Lymphatic drainage is into preauricular, post auricular and superficial cervical lymph nodes.

Nerve Supply Auriculotemporal nerve, great auricular nerve, auricular branch of vagus and the facial nerve supply the ear.

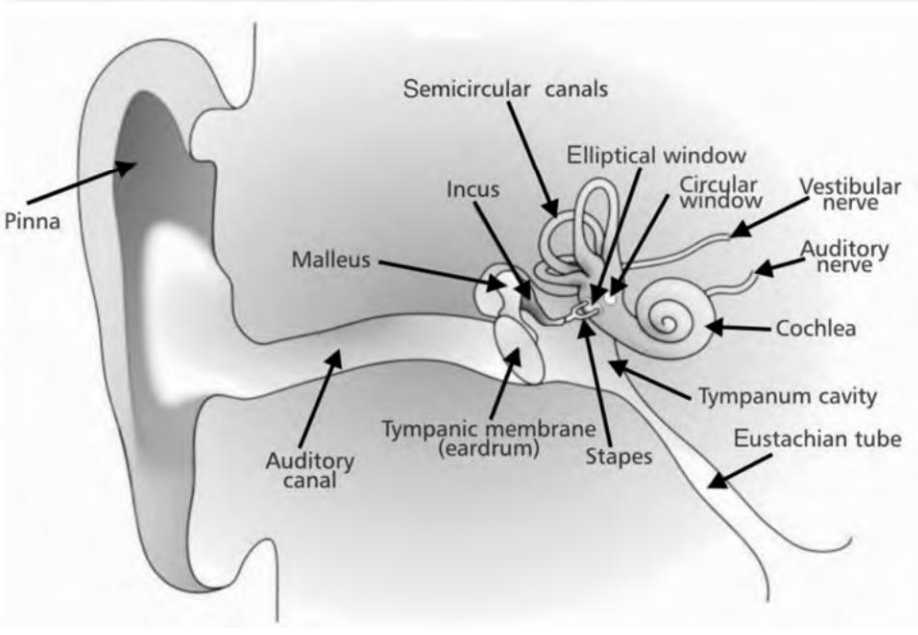


Fig. 11.8 *Auricle*

(b) External Acoustic Meatus or Auditory Canal

The external acoustic meatus is a tube running from the outer ear to the middle ear. It conducts sound waves from the concha to the tympanic membrane. It is 'S' shaped and is 2.5 cm long and 7 mm in diameter.

It is divided into two parts. The cartilaginous part forms the outer third of the canal which is the continuation of the cartilage framework of the pinna while the bony part forms the inner two thirds. Due to the obliquity of the tympanic membrane, the anterior wall and floor are longer than the posterior wall and the roof.

Size and shape of the canal vary among individuals. This is an important factor to consider when fitting hearing aids.

The meatus is lined with skin and is continuous with the skin of the auricle. It contains hairs and numerous sebaceous and ceruminous glands (modified sweat glands), in the skin of lateral third of canal. Ceruminous glands secrete cerumen (wax). Foreign particles like insects, microbes and dust are filtered by the wax and hairs and prevented from reaching the tympanic membrane.

Blood Supply Superficial temporal, posterior auricular and deep auricular branch

Lymphatic Drainage Lymphatic drainage is into the preauricular, post-auricular and superficial cervical lymph nodes

Nerve Supply Auriculo temporal and vagus nerves

Applied Anatomy

(1) For examination of the tympanic membrane, the auricle should be drawn upwards, backwards and laterally.
(2) Boils and infections of the external ear cause little swelling but are very painful due to fixity of skin to the underlying bone and cartilage.
(3) Irritation of the auricular branch of the vagus in the external ear may reflexly produce persistent cough, vomiting or even death due to sudden cardiac inhibition. On the other hand, mild stimulation of this nerve may reflexly produce increased appetite.

2. *Tympanic Membrane (Eardrum)*

The tympanic membrane is a thin translucent membrane that separates the external ear from the middle ear. Its function is to transmit sound from the air to the ossicles inside the middle ear. It is oval in shape.

It is a three-layered structure consisting of the following:

- The outer layer of skin is continuous with the skin of auditory meatus.
- The middle layer of fibrous tissue which thickens laterally to form the annulus, an incomplete ring, and attached to surrounding bone. Superiorly, this ring is deficient and this area is known as the **pars flaccida**. The majority of the drum is composed of the **pars tensa** which is tightly stretched.
- The inner lining of mucous membrane is continuous with that of the middle ear and consists of a single layer of squamous epithelial cells.

The inner surface provides attachment to the handle of malleus. At the circumference, the membrane is fixed to the sulcus in the temporal bone.

Applied Anatomy The membrane on illumination shows the above-mentioned structures.

If damaged, the tympanic membrane can be repaired by a procedure called **tympanoplasty**.

If fluid accumulates within the middle ear as a result of infection or for some other reason, it can be drained by puncturing the tympanic membrane with a small bore needle (tympanocentesis).

3. *Middle Ear—tympanic Cavity—tympanum*

The middle ear is an irregular, laterally compressed space within the petrous part of the temporal bone. It is filled with air, which is conveyed from the nasal part of the pharynx through the auditory (Eustachian) tube.

It contains a chain of movable bones which connect its lateral to its medial wall and serve to convey the vibrations communicated to the tympanic membrane across the cavity to the internal ear.

The cavity of the middle ear is biconcave as the medial and lateral walls are closest to each other in the center.

It consists of two parts: the tympanic cavity proper, opposite the tympanic membrane and the attic or epitympanic recess, above the level of the membrane. The epitympanic recess contains the upper half of the malleus and the greater part of the incus.

Anteriorly, it communicates with the nasopharynx through the auditory tube and posteriorly with the mastoid antrum and air cells through the opening to mastoid antrum.

The cavity, its contents and the air sacs, which open into it, are lined with simple squamous or cuboidal epithelium. The epithelium forms several folds which project into the cavity giving it a honey-combed appearance.

(a) Contents of the Middle Ear

1. Three small bones or ossicles
2. Ligaments of ossicles
3. Two muscles—tensor tympani and stapedius
4. Vessels
5. Nerves—chorda tympani and tympanic plexus

(b) Boundaries

1. Roof and floor are formed by the temporal bone.
2. The anterior, or carotid, wall is narrow. The inferior part is formed by a thin plate of bone and separates the middle ear from internal carotid artery.

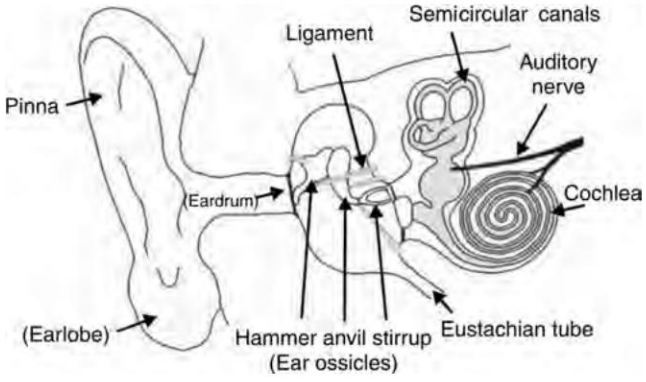


Fig. 11.9 *Structure of the ear*

3. Lateral wall separates middle ear from external auditory meatus and is formed mainly by the tympanic membrane and partly by squamous temporal bone.
4. The posterior wall from above downwards is formed by
   (i) Epitympanic recess which communicates with mastoid antrum through an opening
   (ii) Fossa incudis
   (iii) The pyramid, a conical projection near the junction of the posterior and medial walls
   (iv) Posterior canaliculus for chorda tympani
5. Medial wall separates middle ear from internal ear. It contains
   1. A rounded bulging called promontory
   2. Oval window
   3. Prominence of the facial nerve
   4. Rounded window
   5. Sinus tympani—a depression behind the promontory
   6. A curved lamina

The oval window is covered by a part of stapes and the round window by a thin sheet of fibrous tissue.

(c) Functions

1. Air is present on both sides of the tympanic membrane and pressure is maintained at the level of atmospheric pressure by the Eustachian tube. Sound waves are transmitted from the external ear to the internal ear through the chain of ear ossicles to the tympanic membrane which vibrates when sound waves strike. Air-borne vibrations are transmitted from the tympanic membrane to liquid borne vibrations in the internal ear.
2. Intensity of sound waves is increased ten times by the ossicles. Frequency does not change.

Arterial Supply Anterior and posterior tympanic branches and small arteries like superior and inferior tympanic.

Venous Drainage Venous drainage is into the superior petrosal sinus and pterygoid plexus.

Nerve Supply Tympanic plexus formed by

1. Tympanic branch of glossopharyngeal nerve
2. Superior and inferior caroticotympanic nerves from sympathetic plexus

(d) Applied Anatomy

1. Throat infections spread to middle ear through the auditory tube.
   Pus from the middle ear can take any one of these pathways:
   (a) Tympanic membrane ruptures and pus comes out of the external ear.
   (b) It can erode the roof and enter the cranial cavity and can cause meningitis and brain abscess.
   (c) It can erode the floor and spread downwards.
   (d) It can spread backwards causing mastoid abscess and thrombosis in the sigmoid sinus.
   Chronic otitis media and mastoid abscess are common causes for persistent pus discharge from the ear.
2. Fractures of middle cranial fossa break the roof and rupture the tympanic membrane and can cause bleeding from the ear.

4. Ear Ossicles (Auditory Ossicles)

The ossicles are the three smallest bones in the human body. They are contained within the middle ear space and serve to transmit sounds from the air to the fluid-filled labyrinth (cochlea).

They are malleus, incus and stapes.

(a) Malleus It is so named because it is shaped like a hammer. It is the largest and most laterally placed and has the following parts—head, neck, anterior process, lateral process and handle. The head articulates posteriorly with the body of incus, while the handle lies in contact with the tympanic membrane.

(b) Incus It is an anvil (used by blacksmiths)–shaped bone. It resembles a molar tooth. It has the following parts—body, the long process and the short process. The body articulates with the head of malleus and the long process articulates with stapes. The short process is fixed to the posterior wall of the tympanic cavity by fibrous tissue.

(c) Stapes Stapes is so called as it is shaped like a stirrup. It is the smallest and most medially placed ossicle of the ear. It consists of a head which articulates with the incus, and a neck which gives insertion to the tendon of stapedius. It has two limbs which diverge from the neck and are attached to the foot plate. The footplate is oval in shape and fits into the oval window.

The three ossicles are connected together by fine ligaments.

5. Inner Ear

The inner ear includes the organ of hearing (the cochlea) and a sense organ (labyrinth or vestibular apparatus), that controls balance. It is encased in the petrous part of the temporal bone. Within the cochlea are three fluid-filled spaces: the tympanic canal, the vestibular canal, and the middle canal.

The inner ear consists of a complex series of tubes. The bony tubes (the bony labyrinth) are filled with a fluid called **perilymph** and are lined with periosteum, and in this there are a second series of tubes made out of delicate cellular structures (membranous labyrinth). The fluid inside these membranous structures is called **endolymph**.

(a) Bony Labyrinth It consists of one vestibule, one cochlea and three semicircular canals.

Vestibule It is the expanded part and contains oval and round windows in its lateral wall. It is nearest to the middle ear. Three semicircular canals open into its posterior wall. The medial wall is related to the internal acoustic meatus. (See Fig. 11.10)

(i) Cochlea It is the auditory portion of the inner ear. It appears like a snail's shell. It forms the anterior wall of the labyrinth. The broad base is continuous with the vestibule and the apex winds round a central bony column. A spiral ridge of bone partially divides the cochlear canal into scala vestibuli above and scala tympani below. These two compartments are continuous with each other. The scala vestibuli originates at the oval window and scala tympani at the round window.

The core component of cochlea is the **organ of Corti** in the inner ear that contains auditory sensory cells or hair cells. It contains between 15,000–20,000 auditory nerve receptors. Each receptor has its own hair cell. These nerve cells respond to stimulus or vibrations and send a tiny voltage pulse called an action potential down the associated nerve fiber (axon). These impulses travel to the auditory areas of the brain for processing. The auditory receptors are dendrites of efferent nerves which are part of the 8th cranial nerve—the vestibulocochlear nerve.

(ii) Semicircular Canals There are three bony semicircular canals—anterior or superior, posterior and lateral.

They are set at right angles to each other. Each canal describes two thirds of a circle and is dilated at one end to form the ampulla. They open into the vestibule by 5 openings.

The anterior semicircular canal lies in a vertical plane at right angles to the long axis of the petrous temporal bone. Its posterior end unites with the upper end of the posterior canal.

The posterior semicircular canal also lies in the vertical plane. Its ampulla lies at its lower end. The upper end joins the anterior canal.

The lateral semicircular canal lies in the horizontal plane. Its ampulla lies anteriorly close to the ampulla of the anterior canal.

The lateral semicircular canals of the two sides lie in the same plane, while the anterior canal of one side lies in the plane of the posterior canal of the other side.

The role of the semicircular canal system is to keep the eyes still in space while the head moves around them.

(b) Membranous Labyrinth It is lodged within the bony labyrinth. It is smaller and is partly separated from the bony walls by the perilymph. In certain places, it is fixed to the walls of the cavity.

The membranous labyrinth contains a fluid, the **endolymph**, and on its walls the ramifications of the acoustic nerve are distributed.

The membranous labyrinth is also the location for the receptor cells found in the inner ear.

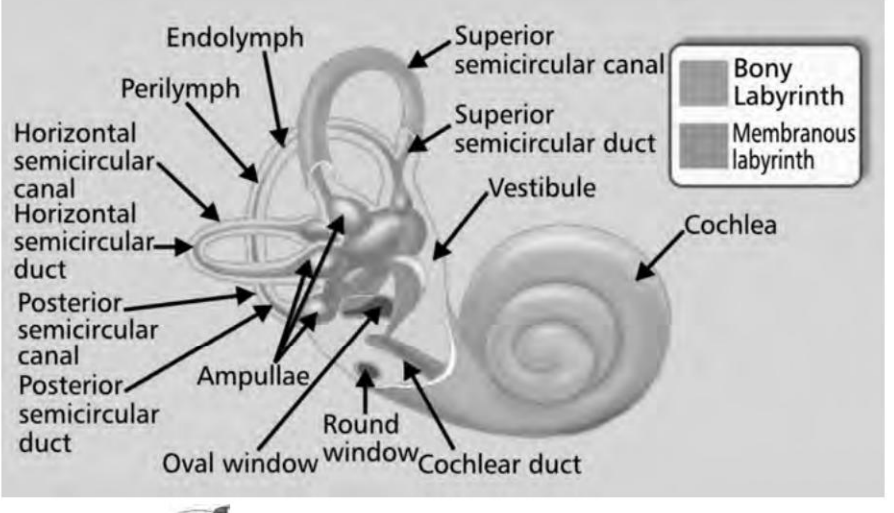


Fig. 11.10 *Inner ear (Refer colour figure)*

A part of the epithelium is specialized to form receptors for sound, a part of it for static balance and a part of it for kinetic balance.

The vestibular system includes the saccule, utricle and the three semicircular canals.

(i) Saccule and Utricle The utricle and saccule are the otolith organs situated in the vestibule between the semicircular canals and cochlea and are sensitive to linear acceleration. The sensory portion of the otolith organs is the macula which is innervated by the vestibular nerve.

The saccule communicates with the cochlear duct through the ductus reunions, and with the utricle through the utriculosaccular duct from which the endolymphatic duct arises.

Each organ has a sheet of hair cells (the macula), whose cilia are embedded in a gelatinous mass. The hair cells are polarized, but they are arrayed in different directions so that a single sheet of hair cells can detect motion, forward and back and side to side. The utricle lies horizontally in the ear, and can detect any motion in the horizontal plane. The saccule is oriented vertically, so it can detect motion in the sagittal plane.

(ii) Spiral Duct It occupies the middle part of the cochlear canal. The floor is formed by the basilar membrane which supports the spiral organ of Corti. The roof is formed by the vestibular membrane and outer wall by the bony wall of cochlea.

Sound waves reaching the endolymph, through the vestibular membrane, make appropriate parts of the basilar membrane to vibrate, so that different parts of the organ of Corti are stimulated by different frequencies of sound. Loudness of sound depends on the amplitude of vibration.

11.2.2 Physiology of Hearing

Every sound produces sound waves in the air which travel at the speed of 332 m/s. The external ear directs the sound waves towards the tympanic membrane, causing it and the ossicles to vibrate. As the central area of the tympanic membrane is connected to the malleus, it also starts vibrating which is transmitted to the oval window through the incus and stapes.

The surface of the eardrum is much larger than the oval window; hence, the vibrations are delivered with greater force to the inner ear.

If a sound is too loud, muscles in the middle ear constrict to reduce the effects of the sound as an attempt to protect the inner ear. If the sound is very loud and too close to the ear, it could damage the hair cells resulting in deafness.

Fluid offers more resistance than air and requires greater force to pass. Amplifying the sound increases the energy which helps the vibrations to pass through the fluid of the inner ear.

At their medial end, the footplate of the stapes rocks to and fro in the oval window and sets up fluid waves in the perilymph, and pressure is increased and transmitted to the cochlear duct. This results in the motion of the hair cells on the basilar membrane which vibrates against the tectorial membrane displacing the cilia on the hair cells.

This results in a chemical reaction within the hair cells and causes electrical responses in the auditory nerve. The louder or more intense the sound, the more impulses are set off. These nerve impulses are transmitted through the cochlear portion of the vestibulocochlear nerve to the hearing area in the temporal lobe in the cerebrum, where sound is perceived.

Sound waves have pitch and volume. Pitch is determined by the frequency of sound waves. Volume depends on the amplitude of sound waves.

1. Types of Conduction

Conduction of sound waves through ossicles is the main pathway in normal hearing.

Conduction from tympanic membrane to the oval window through the air in the middle ear is called **air conduction.**

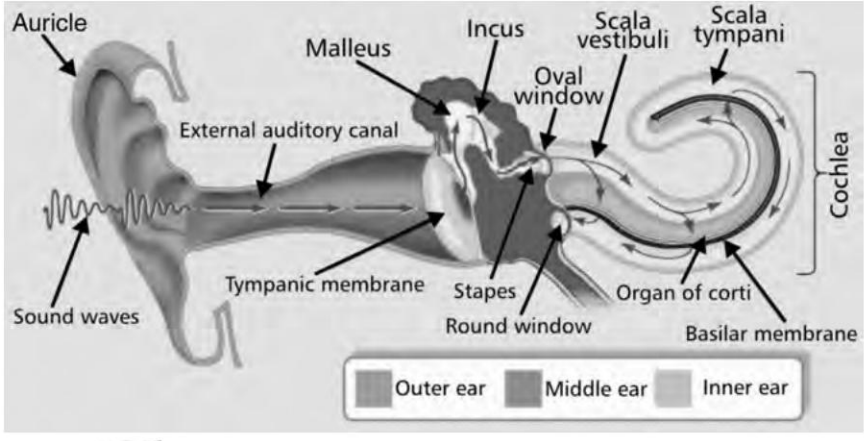


Fig. 11.11 *Physiology of hearing (Refer colour figure)*

Bone conduction is the conduction of sound to the inner ear through the bones of the skull.

2. Hearing Defects

Impairments in hearing can happen in either frequency or intensity or both. Hearing-loss severity is based on how well a person can hear the frequencies or intensities most often associated with speech. Severity can be described as mild, moderate, severe or profound. The term 'hard of hearing' is sometimes used to describe people who have a less severe hearing loss than deafness.

Hearing defects can be of three types:

1. Conductive defect
2. Sensorineural defect
3. Combination of both

Conduction deafness is due to defect in the transmission of sound waves in the external or middle ear. It can occur most commonly due to wax or foreign body in the external auditory canal. Otitis media is another common cause resulting in this type of deafness. Injury or perforation of the tympanic membrane can result in deafness. Otosclerosis can also result in deafness.

Sensorineural deafness occurs when there is damage or disease in the cochlea, organ of Corti, the cochlear branch of vestibular nerve or in the temporal lobe of the brain. The person can hear but cannot understand. It could be congenital, or due to sudden or prolonged noise, or side effect of certain drugs, viz., streptomycin, or due to affection of the auditory pathway by pressure or infection.

3. Methods of Examination

Before carrying out any specific test, a simple procedure is necessary. Test each ear with a wristwatch. First, bring the watch closer to the ear, and ask the person to report when he starts hearing the ticking. Each ear is tested separately and while testing one ear the other ear should be kept closed. The affected ear can be diagnosed. Then it becomes necessary to find out whether the deafness is of conductive type or there is nerve deafness.

(a) Rinne's Test A vibrating fork (256 or 512 cycles per second) is brought near the ear and the patient is asked to report when he stops hearing it. Immediately, it is put on the mastoid process. In conductive deafness, he can hear it over the mastoid process even though he has stopped hearing it through the ear. Normally, he should not be able to hear over the mastoid once he has stopped hearing. In nerve deafness, both the air conduction and bone conduction are decreased but air conduction is still more.

(b) Weber's Test The vibrating fork is put over the center of the forehead and the patient is asked if he can perceive it. Normally, the sound is localized in the center but in conductive deafness, the sound is localized on the affected side. In nerve deafness, the sound is localized to the normal side.

(c) Audiometry

Audiometry is the testing of hearing ability which is performed when hearing loss is suspected.

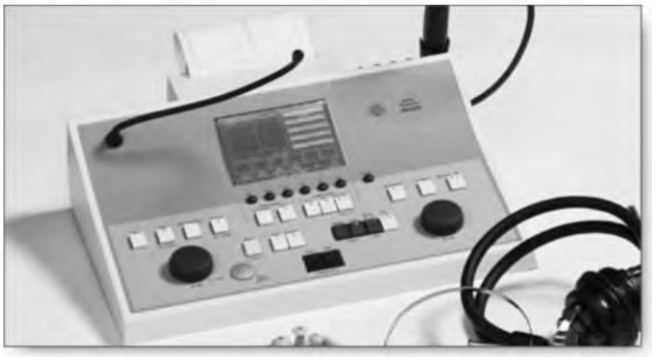


Fig. 11.12 *Audiometry equipment*

It tests mechanical sound transmission (middle-ear function), neural sound transmission (cochlear function), and speech discrimination ability (central function).

This test is carried out with the help of an audiometer and makes use of an audiogram. Results of audiometric tests are used to diagnose hearing loss or diseases of the ear.

Single frequencies are used to test air and bone conduction. Speech testing is also done with an audiometer. The audiometer is an electric instrument consisting of a pure-tone generator, a bone-conduction oscillator for measuring cochlear function, an attenuator for varying loudness, a microphone for speech testing, and earphones for air-conduction testing.

11.2.3 Physiology of Balance

The ability to balance depends on the information received by the brain from the eyes, the muscles, the joints and the vestibular system of the inner ear (the sensory apparatus that helps the body maintain its postural equilibrium). They all send information in the form of nerve impulses from sensory receptors and special nerve endings, to the brain.

The information given by the vestibular system is necessary for coordinating the position of the head and the movement of the eyes. The semicircular canals respond to rotational movements (angular acceleration); while the utricle and saccule respond to changes in the position of the head with respect to gravity (linear acceleration).

The receptor apparatus in the ampulla is crista-ampullaris. Inside each semicircular canal is a sensory receptor called the **cupula**, which is attached to the base. When there is movement

of the head, fluid within the semicircular canals stimulates the cupula and it sends impulses to the brain about the direction of the movement. The utricle and saccule also work similarly. They consist of hair cells or sensory cells embedded in a gelatinous structure. Above the hairs there is an otolith, which has a mass of calcium carbonate crystals, called otoconia. When the body moves up and down or forward and backward, the otoconia causes the sensory cells to bend, which conveys impulses to the brain about the direction of movement.

Thus, the semicircular canals respond to angular movement, while the utricle and saccule respond to linear acceleration and to the direction of gravitational force. The information delivered is proprioceptive in character, dealing with the events within the body itself.

Movement of head causes the flow of endolymph, which results in the deflection of crista-ampullaris. The hairs bend and impulses are generated and are transmitted through the vestibular part of the vestibule-cochlear nerve to the brain. In the same way, the endolymph of saccule and utricle moves the hairs of the hair cells and action potential is generated and transmitted through the vestibular branch to the brain. Thus, crista ampullaris is the sense organ for dynamic equilibrium, which is the maintenance of position of body in response to movement, and macule of utricle and saccule are the sense organs of static equilibrium, which is orientation of the body in relation to gravitational pull.

11.2.4 Disorders

1. Meniere's Disease

Meniere's disease is a disorder characterized by recurrent attacks of hearing loss, vertigo and uncomfortable noise or ringing in the ears called **tinnitus**.

Pathophysiology Meniere's disease is thought to be due to an imbalance in the fluid present in the inner ear. There is a constant balance between secretion and reabsorption of this fluid. Imbalance results due to either an increase in production or decrease in reabsorption of the fluid. The cause of either of this is not known.

2. Acoustic Neuroma

Acoustic neuroma is a slow growing, benign tumor developing on the vestibulo-cochlear nerve. It is also known as vestibular schwannoma. It can cause hearing loss, tinnitus and unsteadiness of gait.

Pathophysiology The exact cause is not known. Usually, it is a slow growing tumor but, occasionally, the growth could be rapid and it could press against the brain and interfere with vital functions.

3. Hearing Loss

Hearing impairment or deafness is a situation when individuals are fully or partially unable to detect or perceive some frequencies of sound.

There are two main types of hearing loss. One type of loss is when sound waves cannot reach the inner ear due to earwax, punctured eardrum or fluid in the ear canal. The other type of hearing loss is permanent and occurs when there is damage to the inner ear or auditory canal.

Hearing impairment is either conductive impairment or sensorineural impairment. It could be unilateral or bilateral.

Conductive deafness is due to dysfunction in any mechanism that conducts sound waves from outside through the outer ear, the eardrum or the middle ear.

Sensorineural deafness is due to dysfunction in the inner ear—the cochlea, the cochlear branch of vestibulocochlear nerve or any area of the brain which processes the signals. Usually, the loss is due to some abnormality in the hair cells of the organ of Corti. The reason could be genetic or developmental abnormality since birth, or due to injury or disease. Virus infection during pregnancy or acute hypoxia at birth could cause this type of deafness in the child.

The person perceives sound at the normal threshold, but cannot discriminate the sounds. He can hear but speech is not understood.

When sensorineural impairment is associated with abnormality of the hearing area in the brain, it is called **central hearing impairment**.

4. Otitis Media

Otitis media is an inflammation of the middle ear. It could be acute or chronic. Inflammation is followed by infection and accumulation of pus leading to bulging of the tympanic membrane, which may even rupture. Pus discharges from the ear or it can also cause mastoiditis and labyrinthitis. Infection can spread through the petrous part of temporal bane and can cause brain abscess and/or meningitis. This is **acute otitis media.**

Pathophysiology The Eustachian tube equalizes the pressure between the outer ear and the middle-ear cavity. It facilitates the drainage of mucus and fluid from the middle-ear cavity. When there is any upper respiratory tract infection or there is infection of the tonsils or adenoids, the Eustachian tube gets inflamed and blocked. Fluid produced by the inflammation cannot be drained and thus collects in the middle ear. This is a good media for the bacteria to multiply and pus is formed.

Children are more commonly affected due to the small size of the Eustachian tube and as they are more frequently affected by tonsillitis and upper respiratory-tract infection. Otitis media is associated more in children on bottle feeding.

Airborne allergies and certain foods can cause otitis media.

Due to any condition involving the bones of the cranium, the cervical canal or temporo-mandibular joint, there could result blockage of Eustachian tube resulting in otitis media.

When the otitis media fails to clear for more than three months, it is called **chronic otitis** media.

If the infection keeps coming frequently off and on, it is called **recurrent otitis media.**

5. *Labyrinthitis*

Labyrinthitis means an inflammation of the inner ear. It causes nausea and vomiting, vertigo, loss of balance and may also be associated with tinnitus, mild headache and some hearing loss. These symptoms worsen with head movements, e.g., getting up from a lying position or looking up.

Pathophysiology The cause in the majority of cases cannot be determined. It is seen after a viral infection especially with common cold.

Injury to the ear or head can cause labyrinthitis.

Bacterial infection of the middle ear can cause serous labyrinthitis due to collection of fluid or suppurative labyrinthitis due to collection of pus.

Alcohol abuse can cause this condition.

Allergies are also thought to be causative.

Certain medicines like aspirin, antibiotics, furosemide can cause labyrinthitis.

A benign tumor of the middle ear can lead to labyrinthitis.

6. *Otosclerosis*

Otosclerosis is an abnormal growth or abnormal bone development near the middle ear. It affects mainly the foot plate of the stapes bone. It joins it to the oval window.

It is usually hereditary and seen more in females than in males, especially during pregnancy. It can result in conductive and/or sensorineural hearing loss.

11.3 PHYSIOLOGY OF SMELL

Smell and taste are closely linked. The taste buds of the tongue identify taste while the nerves in the nose identify smell. Both sensations are communicated to the brain, which integrates the information so that flavors can be recognized and appreciated.

The sense of smell depends on the functioning of not only the olfactory nerve, but also portions of the trigeminal nerve. Qualitative odor sensations like the smell of a rose are mediated by the olfactory nerve while somatosensory odors like irritants like ammonia are mediated by the trigeminal nerve.

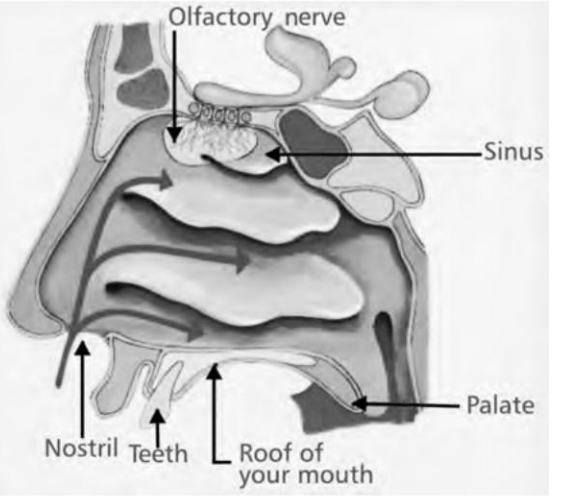


Fig. 11.13 *Physiology of smell*

A small area on the mucous membrane of the olfactory epithelium contains specialized nerve cells called **smell receptors**. There are 10 to 20 million olfactory receptor cells. These cells have dendrites with an expanded end called **olfactory rod**. 10 to 12 cilia arise from the rod which are nonmyelinated and project into the surface of the membrane. The free nerve endings of the trigeminal nerve are located diffusely throughout the nasal epithelium, including regions of the olfactory neuroepithelium.

Axons of the receptors pierce the cribriform plate of the ethmoid bone and reach the olfactory bulb where they synapse. From the bulb, bundles of nerve fibers arise to form the olfactory tract which passes backwards to the olfactory area in the temporal lobe of the cerebral cortex where the impulses are interpreted and odor is perceived.

A particular odor must be in the gaseous form to enter the nasal cavity, during inhalation. It must be sufficiently soluble to dissolve in the fluid covering the olfactory epithelium.

Once odorants enter the nose, they must move to the nasal vault and dissolve within the covering mucous layer in order to stimulate the olfactory receptors. Mucus has an important role in dispersing scents to the underlying receptors. It contains some proteins which increase the actions of odoriferous substances on receptor cells.

The nasal turbinates are also important because they provide moderate resistance and a moist environment, thereby allowing optimal stimulation of olfactory neurons.

The stimulation of the receptors leads to the development of the action potential which causes Na^+ channels to open, and if sufficient Na^+ diffuses into the cell, this leads to depolarization and impulse transmission along the olfactory nerves, and via the olfactory tract to the brain where the electrical potential changes to chemical potential and odor is perceived. The brain interprets the impulse as a distinct odor. The area of the brain

where memories of odor are stored—the middle part of the temporal lobe—is also stimulated.

The air entering the nose is warm; also convection currents carry eddies of inspired air to the roof. Sniffing concentrates volatile molecules in the roof of the nose. So more receptors are stimulated. Sense of smell can increase the appetite. If odors are pleasant, appetite may improve and vice versa. Smell along with the sight of food, increases salivation and stimulates the digestive system.

The fibers of the trigeminal nerve respond to irritating substances like pepper and ammonia and can cause sneezing, unpleasant sensation or shortness of breath.

The sense of smell can create long-lasting memories, e.g., many people remember the hospital smell. When an individual is continuously exposed to an odor, the perception of the odor decreases and ceases in few minutes. Loss of perception is only for that odor and adaptation occurs both in cerebrum and sensory receptors in the nasal cavity. A new odor may be detected at once.

There are a number of distinct odors. Individual odors in a mixed smell can be easily recognized. It is easy to recall an odor that has been experienced only once.

Inflammation of nasal mucosa prevents odorous material from reaching olfactory area of the nose and this leads to loss of sense of smell—anosmia, e.g., in common cold.

The sense of smell in human beings is generally less acute than in other animals. Many animals secrete odorous chemicals called **pheromones** which play an important role in chemical communication, e.g., mating. The role of pheromones in human beings is not much known.

11.4 PHYSIOLOGY OF TASTE

The sense organs for taste are the **taste buds**. In adults, there are about 10,000 taste buds and the number is more in children. In old age, many taste buds degenerate and the sensitivity of taste becomes less.

Most of the taste buds are present on the papillae of the tongue. Taste buds are also situated in the mucosa of epiglottis, palate, pharynx and proximal part of the esophagus.

Taste buds are composed of groups of columnar taste-receptor cells, around 30 to 50 in number. The taste-receptor cells within a bud are arranged in such a way that their tips form a small taste pore, and through this pore extend microvilli from the taste cells. The microvilli of the taste cells bear taste receptors. Interwoven among the taste cells in a taste bud is a network of dendrites of sensory nerves. The nerve fibers form a plexus near the basement membrane and join the nerves. The nerve endings are of facial, glossopharyngeal, and vagus nerves (VII, IX and X cranial nerves). The anterior two thirds

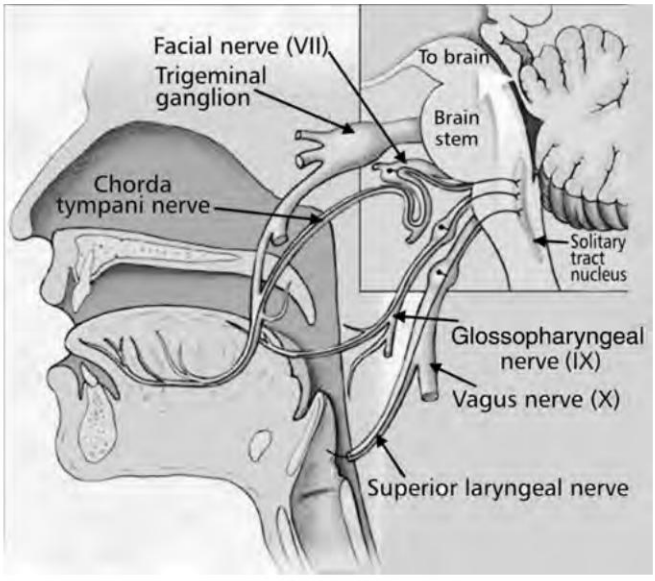


Fig. 11.14 *Physiology of taste*

of tongue is innervated by a branch of facial nerve and posterior one third by glossopharyngeal. The vagus receives impulses from throat and pharynx.

When taste cells are stimulated, by binding of chemicals to their receptors, they depolarize and this depolarization is transmitted to the taste nerve fibers resulting in an action potential that is ultimately transmitted to the brain. Their final destination is the taste area in the parietal lobe of the cerebral cortex where taste is perceived.

There are four primary or fundamental taste sensations, namely,

- Sweet—Mainly at the tip
- Sour—Mainly at the sides
- Bitter—Mainly at the back
- Salt—Mainly at the tip

To create the sensation of taste, a substance has to be in solution form to come in contact with the receptors. Saliva helps to dissolve substances so that they can enter the pores and stimulate the receptors. Perception of taste also appears to be influenced by the thermal stimulation of the tongue. In some people, warming the front of the tongue produces a clear sweet sensation, while cooling leads to a salty or sour sensation.

Sense of taste is impaired if the mouth is dry, as substances can be tasted only if they are in solution. Impairment of the sensation of taste can also result because of poor oral hygiene.

Sense of taste triggers salivation and secretion of gastric juice. It also has a protective function, e.g., with foul-smelling food, reflex gagging or vomiting occurs.

There are various abnormalities of taste, e.g., decrease in taste sensation, loss of taste sensation, disturbance in taste sensation and taste blindness (inability to recognize taste).

REVIEW QUESTIONS

1. Write about the anatomy of the eye.
2. Describe the structure of the retina in detail.
3. Describe the pathway of the optic nerve. Explain briefly the physiology of sight. Describe the effects of lesions at various levels.
4. Name and explain refractive errors of the eye and their correction.
5. Describe the various disorders of the eye.
6. Describe the anatomy of the ear in detail with a diagram.
7. Explain the physiology of hearing. Write a note on hearing defects.
8. Discuss the types of deafness and explain the methods of their detection.
9. Describe the physiology of balance.
10. Write a note on the physiology of taste.
11. Write a note on the physiology of smell.
12. Write short notes on:
    a. Glaucoma
    b. Rods and cones
    c. Ear ossicles
    d. Tympanic membrane
    e. Inner ear
    f. Lens
    g. Interior structure of the eye
    h. Optic nerve
    i. Refractory errors
    j. Cataract
    k. Color blindness
    l. Middle ear
    m. Otitis media

Chapter

12 Endocrine System

- **HORMONES**
  - Types of hormones
  - Control of hormone secretion
  - Mechanism of action of hormones
    - Alteration of the permeability of the cell membrane
    - Activation of intracellular enzyme
    - Action on genes
- **PITUITARY GLANDS**
  - Anatomy
  - Anterior pituitary
    - Physiology
      - Hormones
        - Growth hormone
        - Thyroid stimulating hormone
        - Adrenocorticotrophic hormone
        - Interstitial cell stimulating hormone
        - Prolactin
        - Gonadotropins
          - Follicle stimulating hormone
          - Luteinizing Hormone
  - Posterior pituitary
    - Physiology
      - Antidiuretic hormone
      - Oxytocin
  - Disorders of pituitary gland
    - Gigantism
    - Acromegaly
    - Pituitary dwarfism
    - Simmond's disease
    - Syndrome of inappropriate secretion of ADH

- Diabetes insipidus
- Frohlich's syndrome

- **THYROID GLAND**
  - Anatomy
  - Physiology
    - Synthesis of thyroid hormone
    - Secretion and release of thyroid hormone
    - Regulation of secretion of thyroid gland
  - Disorders of thyroid gland
    - Hyperthyroidism
    - Thyrotoxicosis
    - Hypothyroidism
    - Cretinism
    - Myxedema
    - Goiter
- **PARATHYROID GLANDS**
  - Anatomy
  - Physiology
    - Hormone
    - Regulation of parathormone secretion
    - Action and functions of parathormone
  - Disorders
    - Hypoparathyroidism
    - Hyperparathyroidism
- **ADRENAL GLANDS**
  - Anatomy
    - Adrenal cortex
  - Physiology
    - Hormones
    - Adrenocortical hormones
      - Synthesis
      - Transport and metabolism
    - Glucocorticoids
      - Regulation
      - Actions
    - Mineralocorticoids
      - Regulation
      - Actions
    - Sex hormones
  - Disorders of adrenal cortex
    - Cushing's syndrome
    - Hyperaldosteronism
    - Adrenogenital syndrome
    - Addison's disease
    - Primary adrenal insufficiency

- Secondary adrenal insufficiency
- Addisonian crisis

- Adrenal medulla
  - Physiology
  - Adrenaline and Noradrenaline
    - Regulation
    - Action
  - Disorders
    - Pheochromocytoma
    - Neuroblastoma

- **THYMUS**
  - Anatomy
  - Physiology
    - Lymphoid function
    - Endocrine function
    - Disorder
      - Myaesthenia gravis
- **PINEAL BODY**
- **PANCREAS**
  - Anatomy
  - Physiology
    - Insulin
      - Action
      - Regulation
      - Regulation of blood-glucose level
    - Glucagon
    - Somatostatin
  - Disorders
    - Diabetes mellitus
    - Other forms of diabetes
    - Hypoglycemia

Introduction

In the human body, two systems mainly control the different activities of various organs. They are the nervous system and the endocrine system. Functioning of both is interrelated. Most of the functions of the endocrine organs are controlled by the nervous system, while some of the functions of the nervous system are controlled by hormones.

The endocrine system consists of glands which are situated in different parts of the body and are widely separated from one another without direct anatomical links. The endocrine glands consist of groups of secretory cells surrounded by a fine network of capillaries.

12.1 HORMONES

The endocrine glands secrete their products (hormones), directly into the blood rather than through a duct. Harmones travel to other parts in the body to target organs (which could be quite distant), upon which they act. Hence, they are also known as **ductless glands**.

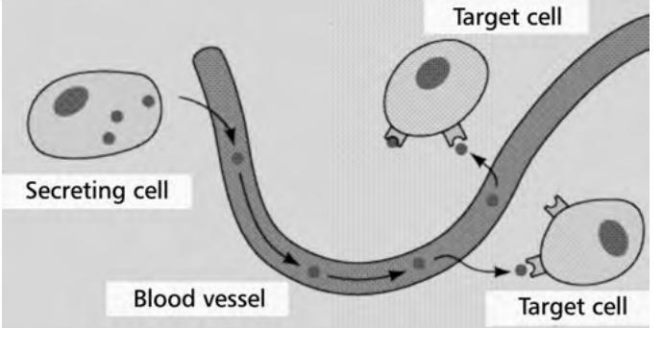


Fig. 12.1 *Ductless glands*

This is how they differ from exocrine glands, e.g., lachrymal glands, salivary glands, etc., which pour their secretions via ducts to the respective organs. The functions of the endocrine glands are mediated by chemical substances called **chemical messengers** (hormones) or **chemical mediators**.

The major glands that make up the human endocrine system are the pituitary, thyroid, parathyroid, adrenals, pineal body, thymus and the reproductive glands, which include the ovaries and testes. The pancreas is also part of this hormone-secreting system, even though it is also associated with the digestive system because it also produces and secretes digestive enzymes.

Once the hormone is secreted, it goes to the target cells. Special proteins bind to some of the hormones and act as carriers that control the amount of hormone that is available to interact with and affect the target cells. When a hormone arrives at the target cell, it binds to a specific area called the **receptor**, where it initiates chemical or metabolic reactions inside the cell, influencing cellular activity, growth and metabolism.

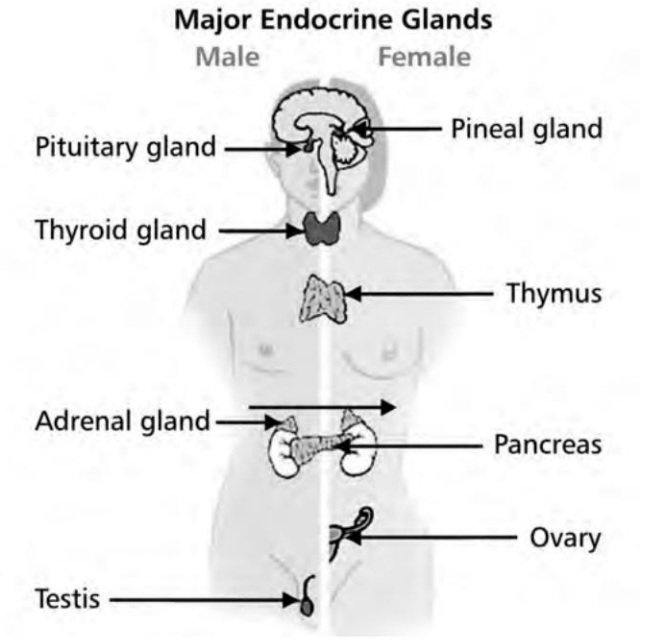


Fig. 12.2 *Major endocrine glands*

The receptors for water-soluble hormones are situated on the cell membrane and those for lipid-soluble hormones are situated inside the cell.

A hormone-receptor-complex is then formed. This complex enters inside the target cell by means of endocytosis and executes the actions. The entire process is called **internalization**. After internalization, some receptors are recycled, while others are replaced by new receptors after some time. When the hormone is in excess, the number of receptors is reduced. This is called **down regulation**. When the hormone is deficient or reduced in amount then the number of receptors is increased. This is called **up regulation**.

12.1.1 Types of Hormones

Hormones are of three types:

1. Steroid hormones
2. Protein hormones
3. Derivatives of the amino acid, tyrosine

Steroid hormones are the corticosteroids and sex hormones.

Protein hormones are the hormones secreted by the pituitary gland, parathyroid glands, pancreas and placenta.

The amino-acid derivatives are the thyroid hormones and adrenal medullary hormones.

12.1.2 Control of Hormone Secretion

The level of hormone in the blood is variable and self-regulating within its normal range. A specific stimulus releases the hormone and then its action reverses or negates the stimulus. This is called **negative feedback mechanism**. This may be controlled directly or indirectly. Direct control is by the blood levels of the stimulus, e.g., insulin. Indirect control is through the release of hormones by the hypothalamus and the anterior pituitary gland.

In the **positive feedback mechanism**, the stimulus is amplified and hormone release is increased till a particular process is complete and then, the stimulus ceases, e.g., release of oxytocin during labor.

12.1.3 Mechanism of Action of Hormones

The hormone combines with the receptor and acts by any one of the following mechanisms.

1. Alteration of the Permeability of the Cell Membrane

The best example is action in a synapse or neuromuscular junction. Acetylcholine, released in response to impulse at the axon terminal, comes out from the vesicles, passes through the presynaptic membrane and enters the synaptic cleft. It reaches the postsynaptic membrane and combines with the receptor protein on the membrane and forms a receptor hormone complex. The complex opens sodium channels so that sodium ions enter from the extracellular fluid. The resting membrane potential is altered and end-plate potential develops.

2. Activation of the Intracellular Enzyme

Protein and peptide hormones, catecholamine like epinephrine, and prostaglandins, find their receptors on the plasma membrane of target cells. They form a receptor hormone complex. Binding of hormone to the receptor initiates a series of events which leads to generation of so-called **second messengers** within the cell (the hormone is the first messenger). They are also called **hormonal mediators**. This complex activates the enzymes of the cell. The second messengers then trigger a series of molecular interactions and have their effect and alter the physiologic state of the cell. The commonest second messenger is cyclic AMP. Protein hormones and catecholamines act through cyclic AMP. Another term used to describe this entire process is **signal transduction**.

3. Action on Genes

Receptors for steroid and thyroid hormones are located inside the target cells, in the cytoplasm or nucleus. Steroid hormones bind with the receptor in the cytoplasm while thyroid hormones bind with the receptor in the nucleus. Once inside the cell, the steroid hormone binds with a specific receptor found only in the cytoplasm of the target cell. The receptor-bound steroid hormone then travels into the nucleus and binds to another specific receptor on the chromatin. Once bound to the chromatin, this steroid hormone-receptor-complex calls for the production of messenger RNA (mRNA) molecules through a process called **transcription**. The mRNA molecules are then modified and transported to the cytoplasm. The mRNA molecules code for the production of proteins through a process called translation.

12.2 PITUITARY GLAND

12.2.1 Anatomy

The pituitary gland is also known as the **hypophysis**. It lies in the hypophyseal fossa of the sphenoid bone, at the base of the brain in the sella turcica, below the hypothalamus and is attached to it with a stalk. It is a small gland, the size of a pea with a diameter of 1 cm and weighs 0.5 g to 1 g. The pituitary gland and the hypothalamus act as a unit and regulate the functions of the other glands.

The pituitary gland regulates many physiological processes. It has two lobes, the frontal (anterior) lobe and the rear (posterior) lobe, which have different functions and are derived from different types of tissue in the embryonic development.

1. The anterior pituitary is also known as **adenohypophysis**.
2. The posterior pituitary is also known as **neurohypophysis** and is a down-growth of nervous tissue from the brain.

There is a network of nerve fibers between the hypothalamus and the posterior pituitary.

Between these two portions is a small, thin strip of avascular tissue called intermediate lobe or **pars intermedia**. This is very small in human beings and its function is not known.

12.2.2 Anterior Pituitary

The anterior pituitary develops from a depression in the dorsal wall of the pharynx and comes out as an upgrowth of the glandular epithelium of pharynx.

1. Physiology

Under the influence of the hypothalamus, the anterior pituitary produces and secretes several peptide hormones that regulate many physiological processes including growth and reproduction.

It also regulates many other endocrine glands; hence it is called the 'master gland' or **Master of the Endocrine Orchestra'**. The hormones secreted by the anterior pituitary

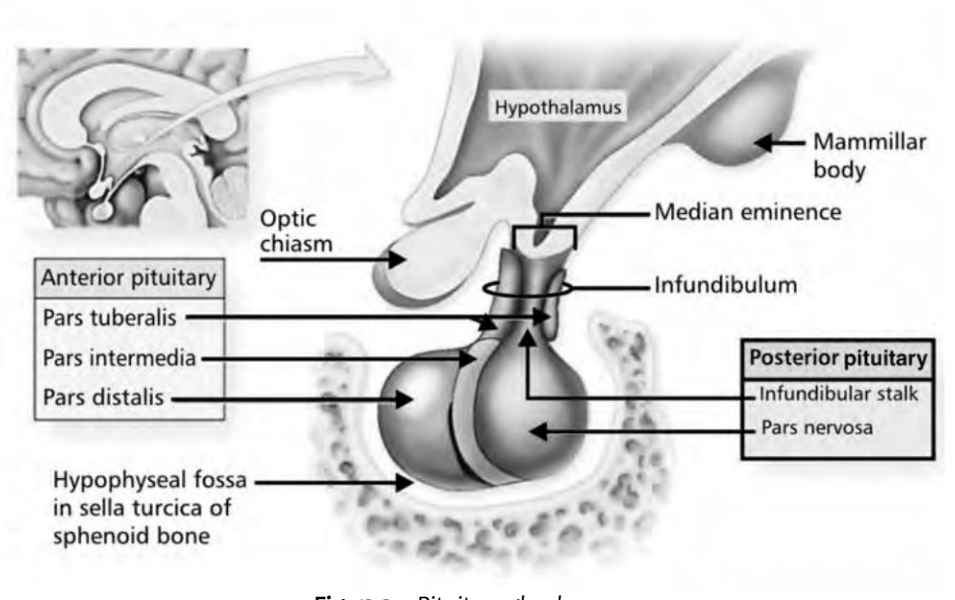


Fig. 12.3 *Pituitary gland*

either stimulate or inhibit secretion of the other endocrine glands or they could have a direct effect on the target organs.

2. *Hormones*

The hormones secreted by the anterior pituitary are

(a) Growth Hormone (GH)
(b) Thyroid Stimulating Hormone (TSH)
(c) Adrenocorticotropic Hormone (ACTH)
(d) Follicle Stimulating Hormone (FSH)
(e) Luteinizing Hormone (LH)
(f) Interstitial Cell Stimulating Hormone (ICSH)
(g) Prolactin

The follicle stimulating hormone and the luteinizing hormone are together called **gonadotropins** as they act on the gonads.

Hypothalamic hormones are secreted and sent to the anterior lobe by way of a special capillary system, called the **hypothalamic-hypophyseal portal system**.

The whole system is controlled by a negative feedback mechanism, e.g., when there is a decreased level of a certain hormone in the blood supplying the hypothalamus, this leads to production of the appropriate stimulating hormone which stimulates the release of a trophic hormone by the anterior pituitary. This stimulates the target gland to produce and release

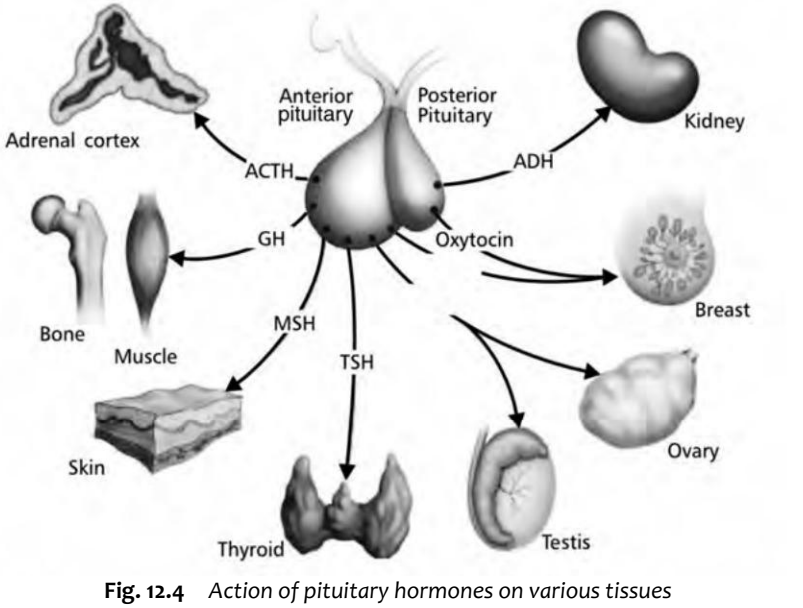


Fig. 12.4 *Action of pituitary hormones on various tissues*

the hormone. So blood level rises. This will now inhibit the secretion of a releasing factor by the hypothalamus.

(a) Growth Hormone (GH) Growth Hormone (GH) is the maximally synthesized hormone by the anterior pituitary. It is a polypeptide hormone which is synthesized, stored, and secreted by the somatotrophs of the anterior pituitary gland.

Action The growth hormone is responsible for the general growth of the body and the growth of almost all the tissues which are capable of growing. It increases the size and the number of cells. It acts by interacting with a specific receptor on the surface of cells.

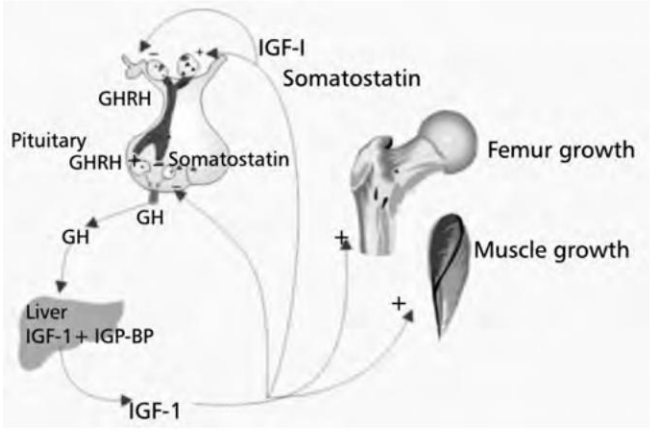


Fig. 12.5 *Hypothalamus and growth*

The growth hormone also acts on the metabolism of proteins, carbohydrates and lipids.

- **Effect of Growth Hormone on Bones and Muscles**
  The growth hormone has a direct effect on bone growth in stimulating differentiation of chondrocytes. It increases the length of the bones till fusion of epiphysis with the shaft takes place, i.e., from puberty onwards up to 21 years. As it stimulates osteoblasts, the bone continues to become thick throughout life; especially, the membranous bones such as the jaw bone and the skull bones.

  It is also the key player in muscle growth. It stimulates both the differentiation and proliferation of myoblasts. It also stimulates amino-acid uptake and protein synthesis in the muscles and other tissues.
- **Effect of Growth Hormone on the Metabolism of Proteins**
  The growth hormone stimulates protein anabolism in many tissues. This effect reflects increased amino-acid uptake, increased protein synthesis and decreased oxidation of proteins. It increases the transport of amino acids through the cell membrane. So, concentration of amino acids in the cells is increased leading to increase in the synthesis of proteins.

  It increases the transcription of DNA to RNA and also increases the translation of RNA in the cells. This also leads to increased synthesis of proteins in the cells.

  The growth hormone inhibits the breakdown of cellular protein; so this also helps in building up of the tissues.

  Thus, growth hormone accelerates the synthesis of proteins.
- **Effect of Growth Hormone on the Metabolism of Carbohydrates**
  Growth hormone is one of the many hormones that serve to maintain blood glucose within a normal range. It is often said to have anti-insulin activity, because it suppresses the abilities of insulin to stimulate uptake of glucose in peripheral tissues and enhance glucose synthesis in the liver. Somewhat paradoxically, administration of growth hormone stimulates insulin secretion, leading to hyperinsulinemia.

  The main action of the growth hormone on carbohydrates is the conservation of glucose. It decreases the peripheral utilization of glucose for energy production and increases the mobilization of fatty acids. More fatty acids are available for production of energy and the peripheral utilization of glucose is reduced. Whatever amount of glucose enters the cells is converted into glycogen. When the concentration of glycogen goes on increasing within the cells, the cells get saturated with glycogen. So, no more glucose can enter into the cells. Finally, glucose level in blood increases. This is called **pituitary diabetes**.

  The increased blood glucose stimulates the beta cells in the islets of Langerhans in pancreas. Also, growth hormone stimulates the beta cells of the islets directly. This leads to a marked secretion of insulin. But, due to excessive stimulation of the beta cells, a stage comes when the beta cells get burnt out. This causes deficiency of insulin, which leads to **true diabetes**. This is known as diabetogenic effect of the growth hormone.
- **Effect of Growth Hormone on the Metabolism of Fats**
  The Growth hormone enhances the utilization of fat by stimulating triglyceride breakdown and oxidation in adipocytes.

  Fat is mobilized from adipose tissue. Concentration of fatty acids increases in the body fluids so that fatty acids are available for the production of energy by the cells; hence, proteins are spared.

  When fatty acids are utilized, acetoacetic acid is formed by the liver in excess. This causes ketosis. Sometimes, there is excessive accumulation of fat in the liver which could lead to fatty liver.

Thus, the function of the growth hormone is to promote tissue growth, especially of bones and muscles. It regulates various aspects of metabolism in many organs; stimulates protein synthesis; promotes breakdown of fats; and increases blood-glucose levels.

Regulation of Growth Hormone Growth-hormone concentration in the blood of a normal adult is up to 300 ng %; in children it is 500 ng %.

Production of growth hormone is modulated by many factors including stress, exercise, nutrition, sleep and the growth hormone itself. However, its primary controllers are two hypothalamic hormones and one hormone from the stomach. One of the hypothalamic hormones is Growth Hormone Releasing Hormone (GHRH) which stimulates the release of the growth hormone. The other hormone is Growth Hormone Inhibitory Hormone (GHIH) which inhibits the secretion of the growth hormone. **Ghrelin** is a peptide hormone secreted from the stomach which binds to receptors on somatotrophs and stimulates secretion of the growth hormone.

Secretion of the growth hormone is reduced when blood-glucose level increases or when concentration of free fatty acid in blood is increased. Secretion of the growth hormone is greater at night during sleep. Exercise and anxiety stimulate its release.

Feedback Control Growth-hormone secretion is under feedback control. GHRH from the hypothalamus causes release of the growth hormone from the anterior pituitary. The growth hormone acts on the tissues of the body. It activates the liver cells to secrete somatomedin-c which suppresses the release of the growth hormone from the anterior pituitary. Somatomedin-c also causes release of GHIH from the hypothalamus.

When the level of growth hormone decreases, GHRH is secreted from the hypothalamus which stimulates the secretion of the growth hormone from the pituitary.

(b) Thyroid Stimulating Hormone (TSH) The thyroid stimulating hormone (also known as TSH or thyrotropin) is a peptide hormone synthesized and secreted by thyrotrophs in the anterior pituitary gland.

Action It regulates the function of the thyroid gland.

Regulation TSH production is controlled by a Thyrotropin Releasing Hormone, (TRH), which is manufactured in the hypothalamus and transported to the anterior pituitary gland via the superior hypophyseal artery, where it increases TSH production and its release. Somatostatin is also produced by the hypothalamus, and has an opposite effect on the pituitary production of TSH, decreasing or inhibiting its release. It is necessary for the growth and activity of the thyroid gland. Its release is lowest in the evening and highest during night.

The level of thyroid hormones (T3 and T4) in the blood has an effect on the pituitary release of TSH. When the levels of T3 and T4 are low, the production of TSH is increased, and conversely, when levels of T3 and T4 are high then TSH production is decreased. Thus, secretion of TSH is regulated by a negative feedback mechanism.

TSH increases the number of cuboidal cells of the thyroid and then converts them into columnar cells and from them thyroid follicles develop. It also increases the secretory activity of the cells of thyroid follicles.

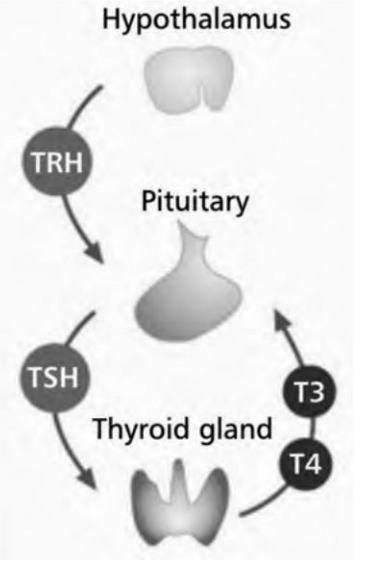


Fig. 12.6 *Regulation of thyroid hormones*

Iodide pump and iodide trapping into the cells is increased. Iodination of tyrosine and coupling to form thyroid hormone is increased. TSH stimulates the thyroid gland to secrete the hormones thyroxine (T4) and triiodothyronine (T3). Release of hormones is increased by increasing proteolysis of thyroglobulin.

(c) Adrenocorticotrophic Hormone (ACTH) Adrenocorticotrophic hormone (ACTH or corticotropin) is a polypeptide tropic hormone produced and secreted by the anterior pituitary gland. It is an important component of the hypothalamic-pituitary-adrenal axis. Its synthesis and release is promoted by a corticotrophin-releasing hormone from the hypothalamus. It is produced in response to biological stress.

ACTH levels are highest in the morning and fall to the lowest around midnight. This circadian rhythm is maintained throughout life. It is associated with sleep patterns. Secretion is regulated by a feedback mechanism.

Its principal effects are increased production of androgens and, as its name suggests, cortisol from the adrenal cortex. It maintains structural integrity and vascularization of the adrenal cortex.

ACTH stimulates the synthesis of and release of glucocorticoids from the adrenal cortex and prolongs the actions of glucocorticoids on different cells.

ACTH also has a melanocyte-stimulating effect due to structural similarity to the Melanocyte Stimulating Hormone (MSH).

It mobilizes fat from the tissues.

(d) Interstitial Cell Stimulating Hormone In males, the luteinizing hormone is called Interstitial Cell Stimulating Hormone (ICSH), as it stimulates Leydig cell production of testosterone.

(e) Prolactin Prolactin (PRL), or Luteotropic Hormone (LTH), is a peptide hormone primarily associated with lactation. It acts directly on the epithelial cells of the mammary glands and causes **alveolar hyperplasia**.

The blood level of prolactin is stimulated by a prolactin-releasing hormone, released from the hypothalamus and is inhibited or lowered by a prolactin-inhibiting hormone.

After birth, suckling by the baby stimulates prolactin secretion and lactation in the mother. It helps in initiating and maintaining lactation.

High prolactin levels tend to suppress the ovulatory cycle by inhibiting the secretion of both Follicle Stimulating Hormone (FSH) and Gonadotrophin-Releasing Hormone (GnRH). Hence, a high blood level of prolactin reduces the incidence of conception during lactation period.

Prolactin levels peak during REM sleep and in the early morning. Levels can rise after exercise, meals, sexual intercourse or minor surgical procedures. Emotional stress increases its production.

(f) Gonadotropins The two principal gonadotropins are the Luteinizing Hormone (LH) and the Follicle Stimulating Hormone (FSH). Both hormones consist of two peptide chains. Gonadotropins are released under the control of Gonadotrophin-Releasing Hormone (GnRH) from the hypothalamus.

The gonads—testes and ovaries—are the primary target organs for LH and FSH. They affect multiple cell types and elicit multiple responses from the target organs. LH stimulates the Leydig cells of the testes and the theca cells of the ovaries to produce testosterone (and indirectly estradiol). FSH stimulates the spermatogenic tissue of the testes and stimulates the production of sperm in the testes.

Gonadotropins stimulate the granulosa cells of the ovarian follicles and help in the process of maturation of the ovarian follicle.

12.2.3 Posterior Pituitary

The posterior pituitary consists, mainly, of neuronal projections (axons) extending from the supraoptic and paraventricular nuclei of the hypothalamus that secrete peptide hormones into the capillaries of the hypophyseal circulation. The axons or nerve fibers form a bundle called the **hypothalamohypophyseal tract**. The endings form knobs. The posterior pituitary also contains a specialized type of astrocytic glial cell called pituicytes.

Physiology

The hormones of the posterior pituitary are Antidiuretic Hormone (ADH) and oxytocin. They are synthesized in the nerve cell bodies and transported along the axons and stored in the knobs.

The release of these hormones is stimulated by impulses from the hypothalamus and their action is on non-endocrine tissues like kidneys.

(a) Antidiuretic Hormone (ADH) The antidiuretic hormone is also known as **vasopressin**. The main effect of ADH is to reduce urine output. It also produces constriction of blood vessels. But the amount required to produce vasoconstriction is much higher than the quantity required for antidiuretic effect. So, it is aptly called the antidiuretic hormone.

It is a peptide hormone formed in the hypothalamus, and then transported via axons to, and released from, the posterior pituitary.

ADH has two principle sites of action—the kidneys and blood vessels.

The primary function of ADH is to regulate extracellular fluid volume by increasing the reabsorption of water in the kidneys, although it is also a vasoconstrictor and pressor agent (hence, the name 'vasopressin'). It acts on renal collecting ducts by acting on V_2 receptors to increase water permeability from the distal convoluted tubule and collecting duct in the kidney. Hence, the reabsorption of water from the glomerular filtrate is increased which leads to decreased urine output (the antidiuretic action). This increases blood volume, cardiac output and arterial pressure.

In the absence of ADH, reabsorption of water in the renal tubules does not occur. Thus, the urine produced is dilute and a large amount of urine is excreted. This is called diuresis and the disease is called **diabetes insipidus**.

A secondary function is vasoconstriction. It binds to V_1 receptors on vascular smooth muscle to cause vasoconstriction, which increases arterial pressure; however, the normal physiological concentrations are below its vasoactive range. In severe blood loss or in hypovolemic shock, when vasopressin release is very high, it does contribute to the compensatory increase in systemic vascular resistance. There is constriction of all the arteries of the body, specifically arteries of the skin and an abdominal organ; thereby it helps in maintaining the blood pressure.

Regulation of Secretion of Antidiuretic Hormone

Vasopressin is secreted from the posterior pituitary gland in response to

- Reduction in plasma volume

- Increase in the plasma osmolality
- Cholecystokinin by the small intestine

Secretion in response to reduced plasma volume is activated by pressure receptors in the veins, atria, and carotids. When there is decrease in the volume of extracellular fluid, as seen in dehydration or after hemorrhage, it leads to increase in osmolar concentration in extracellular fluid. The osmoreceptors are stimulated and this leads to secretion of ADH. More water is reabsorbed and urine output decreases. The body retains more water and the osmotic pressure decreases.

When osmotic pressure decreases, e.g., after a large amount of fluid intake, ADH secretion is inhibited; less water is reabsorbed and urine output increases and the osmotic pressure returns to normal.

Secretion in response to increases in plasma osmotic pressure is mediated by osmoreceptors in the hypothalamus. The neurons that make vasopressin, in the hypothalamicsupraoptic nuclei and paraventricular nuclei, are themselves osmoreceptors,

Secretion in response to increases in plasma cholecystokinin is mediated by an unknown pathway.

(b) Oxytocin Oxytocin is made in the magnocellular neurosecretory cells of the supraoptic and paraventricular nuclei of the hypothalamus. It is transported via the nerve fibers and is stored at the axon terminals in the posterior pituitary. It is released into the blood when suitable stimuli reach the posterior pituitary from the hypothalamus.

Oxytocin stimulates two target tissues during and after parturition, i.e., childbirth. They are the uterine smooth muscles and the cells of the lactating breast.

Milk ejection involves a positive feedback mechanism. When the child suckles the nipple, sensory impulses are generated which are transmitted to the hypothalamus. This triggers the release of oxytocin from the posterior pituitary. Oxytocin, which is released, stimulates the contraction of myoepithelial cells causing milk to be ejected into the ducts and cisterns from the alveoli of the mammary glands.

During parturition (childbirth), the release of oxytocin from the posterior pituitary becomes manifold. This is in response to the distention of cervix and stimulation of sensory stretch receptors. When the fetus comes down the cervix, the receptors in the cervix are stimulated and they discharge impulses which stimulate the posterior pituitary to release more hormone. This in turn, stimulates the uterine muscles which enhance contraction of uterine smooth muscle and leads to more forceful uterine contractions to facilitate birth and the cervix gets stretched further. This is due to positive feedback mechanism. As soon as the baby is delivered, the distention of the cervix decreases and oxytocin secretion is inhibited.

Both these reflexes are called **neuroendocrine reflexes** because the reflex is initiated by the nervous factors and completed by means of hormones.

The role of oxytocin in males and in nonlactating females is not clear.

The action of oxytocin on the nonpregnant uterus is to facilitate the transport of sperms through the female genital tract up to the Fallopian tube by causing uterine contraction during sexual intercourse. The vaginal receptors get stimulated during sexual intercourse, and generate impulses which go to the hypothalamus, and oxytocin is released which acts on the uterus leading to its contraction.

12.2.4 Disorders of the Pituitary Gland

The disorders of endocrine glands are either due to defective growth or due to auto-immune diseases and the effects, that result, are either due to increased secretion or inhibited secretion.

The disorders of the pituitary gland are

1. Hypersecretion of anterior pituitary:
   - Gigantism
   - Acromegaly
2. Hyposecretion of anterior pituitary:
   - Pituitary dwarfism
   - Simmond's disease
3. Hypersecretion of posterior pituitary: Syndrome of inappropriate hypersecretion of antidiuretic hormone
4. Hyposecretion of posterior pituitary: Diabetes insipidus
5. Hypoactivity of both anterior and posterior pituitary: Frohlich's syndrome

1. Gigantism

Gigantism is characterized by excessive growth and height. It occurs due to prepubertal excess of the growth hormone while the epiphyseal cartilages of the long bones are still growing and the epiphysis has still not fused with the shaft.

Fig. 12.7 *Gigantism*

It starts from adolescence. The child will grow in height, and there is excess growth of the muscles and organs.

Other symptoms include delayed puberty, thickening of the facial features, large hands and feet with thick fingers and toes. Menstruation is irregular in females. There is increased sweating and increased BMR.

Such people also develop glycosuria and pituitary diabetes. The hyperglycemia stimulates the beta cells of the islets of Langerhans and there is release of insulin. The over-activity of the beta cells of Langerhans causes their degeneration and insulin secretion is reduced. Finally, diabetes mellitus develops.

Ultimately, there is burning out of the cells of the anterior pituitary and there is hypopituitarism.

2. Acromegaly

Acromegaly is a syndrome that results when the pituitary gland produces excess growth hormone after epiphyseal plate closure. A number of disorders may affect the pituitary but the most common is **pituitary adenoma**. It starts from puberty.

Fig. 12.8 *Acromegaly*

There is soft-tissue swelling resulting in enlargement of the hands, feet, nose, lips and ears, and a general thickening of the skin. There is also enlargement of membranous bones like cranium, nose, supraorbital ridges and the lower jaw. The bones become abnormally thick and broad. The facial features are coarse and the tongue is enlarged. The vocal cords are also thickened resulting in a characteristic thick, deep voice and slowing of the speech.

The viscera are enlarged. Thyroid gland, parathyroid glands and adrenals show hyperactivity. There is development of diabetes mellitus causing hyperglycemia and glycosuria.

3. Pituitary Dwarfism

Pituitary dwarfism is caused by dysfunction of the pituitary gland. It is due to severe deficiency of the growth hormone and is a childhood disorder. There is growth retardation, and these persons are very short but have normal body proportions except that the head is slightly larger.

A few children go through delayed, but normal puberty and have normal reproductive capabilities. Others never become sexually mature.

Tumor, genetic abnormality, atrophy of acidophilic cells or deficiency of growth hormone releasing hormone from the hypothalamus could be one of the causes.

There are two types of pituitary dwarfism:

- **Panhypopituitarism** is due to a deficit of all of the anterior pituitary hormones in which puberty is delayed or the affected persons do not attain puberty. There is proportionate, generalized slow growth. This accounts for about 2/3 of pituitary dwarfism cases.

Fig. 12.9 *Dwarfism*

- **Pituitary dwarfism** is due to an isolated deficiency of GH and accounts for about 1/3 of cases. There is perfectly proportioned growth. They mature sexually and reproductive function is not affected. Mental activity is normal.

4. Simmond's Disease

In Simmond's disease, there is hyposecretion of all anterior pituitary hormones. Panhypopituitarism occurs in which cachexia is a prominent feature and is called **pituitary cachexia**. It occurs due to atrophy, destruction or degeneration of the anterior pituitary.

The subject appears senile. There is loss of hair and teeth. The face is wrinkled and there is extreme emaciation.

5. Syndrome of Inappropriate Hypersecretion of Antidiuretic Hormone

The Syndrome of Inappropriate Antidiuretic Hormone Hypersecretion (SIADH) is a condition commonly found in patients being hospitalized for central nervous system injury. It is characterized by excessive release of antidiuretic hormone (ADH or vasopressin) from the posterior pituitary gland and results in hyponatremia, and sometimes fluid overload.

6. Diabetes Insipidus

Diabetes Insipidus (DI) is a condition characterized by excessive thirst and excretion of large amounts of severely diluted urine. It may be caused by a deficiency of antidiuretic hormone (ADH). It results from damage to the pituitary gland, which disrupts the normal storage and release of ADH. It could also be caused by an insensitivity of the kidneys to ADH. Rarely, it can be induced iatrogenically by various drugs.

There is deficiency of reabsorption of water by the renal tubules. In the absence of ADH, the epithelial cells of the distal convoluted tubule and the collecting duct become impermeable to water. So there is excretion of large amounts of dilute urine. This is called **polyuria**. This leads to loss of water from the body leading to excessive thirst. So water intake is markedly increased because the rapid loss of water activates thirst mechanism in the hypothalamus. This is called **polydipsia**.

Sometimes diabetes insipidus is referred to as 'water' diabetes to distinguish it from the more common diabetes mellitus or 'sugar' diabetes.

The thirst center in the hypothalamus is also, sometimes, affected by the lesion. So water intake is reduced in these patients, which is not compensated and dehydration develops which may sometimes end in death.

7. Frohlich's Syndrome

It is a rare childhood metabolic disorder characterized by obesity, growth retardation, retarded mental development and retarded development of the genital organs.

It develops due to panhypopituitarism and there is deficiency of growth hormone, follicle stimulating hormone and luteinizing hormone.

It is usually associated with tumors of the hypothalamus. There is increased appetite, and obesity and sterility are seen in adults.

12.3 THYROID GLAND

12.3.1 Anatomy

The thyroid gland is a butterfly-shaped organ and composed of two lobes connected in the middle by the isthmus. The lobes lie on either side of the thyroid cartilage. The organ is situated on the anterior side of the neck, lying in front and around the larynx and trachea at the level of 5th, 6th and 7th cervical and 1st thoracic vertebrae reaching posteriorly up to the esophagus and the carotid sheath. It starts cranially at the oblique line on the thyroid cartilage and extends inferiorly to the fourth to sixth tracheal ring. Two parathyroid glands lie against the posterior surface of each lobe.

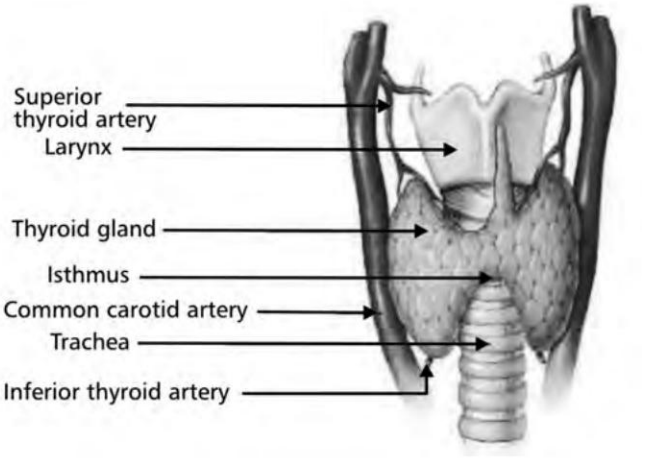


Fig. 12.10 *Thyroid gland*

It is a highly vascular gland, weighs about 20 to 40 grams in an adult and is covered by a fibrous sheath. It is larger in females than in males. The function of the thyroid gland is increased during pregnancy and lactation and decreased during menopause. Diseases of the thyroid gland are also more common in females.

The thyroid is composed of cuboidal epithelium which forms spherical follicles that selectively absorb iodine from the blood for production of thyroid hormones. Twenty-five per cent of all the body's iodide ions are in the thyroid gland. Inside the follicles, the colloid serves as a reservoir of materials for thyroid hormone production and, to a lesser extent, acts as a reservoir for the hormones themselves. Colloid is rich in a protein called **thyroglobulin**.

(a) Arterial Supply The arterial blood supply is through the superior and inferior thyroid arteries; branches of subclavian artery.

(b) Venous Drainage The venous return is by the thyroid veins which drain into the internal jugular veins.

(c) Nerve Supply The gland is supplied by sympathetic nerve input from the superior cervical ganglion and the cervicothoracic ganglion, and by parasympathetic nerve input from the superior laryngeal nerve and the recurrent laryngeal nerve.

(d) Lymphatic Drainage Lymphatic drainage is into the lateral deep cervical lymph nodes and the pre- and paratracheal lymph nodes.

12.3.2 Physiology

The primary function of the thyroid is production of the hormones thyroxine (T_4), triiodothyronine (T_3), and calcitonin. Up to 80% of T_4 is converted to T_3 by peripheral organs such as the liver, kidney and spleen. T_3 is about ten times more active than T_4.

1. Synthesis of Thyroid Hormone

Iodine and tyrosine are essential for the formation of thyroid hormones. This is available from seafood, vegetables and table salt.

The basal membrane of the thyroid cells has a specific ability to transport the iodine from the blood into the interior of the cell. This is called **iodine trapping**. Once inside the cell, iodide is transported into the lumen of the follicle along with thyroglobulin.

The concentration of iodide is 30 times more in the thyroid gland than in the blood. Combination of iodine with tyrosine takes place. This is known as iodination. The enzyme peroxidase, secreted in the follicular cells, accelerates the process. Iodination of tyrosine occurs in several stages and finally tetraiodothyronine or thyroxine is formed. Inactivity of peroxidase could stop production of the thyroid hormone.

The thyroid hormones are synthesized as large precursor molecules called thyroglobulin, the major constituent of colloid. The hormone is still tied up in molecules of thyroglobulin and remains in the form of vesicles along with thyroglobulin. Thyroid hormones are liberated from their thyroglobulin by lysosomal digestion in thyroid epithelial cells. The thyroid hormone can be stored for several months.

2. Secretion and Release of Thyroid Hormone

Lysosomes of the cells fuse with the vesicles. Lysosomes contain digestive enzymes like proteinases which digest the thyroglobulin and release the hormones. The hormone diffuses through the base of the follicular cells and enters the capillaries.

The chief stimulator of thyroid-hormone synthesis and release is the thyroid-stimulating hormone from the anterior pituitary which itself is stimulated by the Thyroid Releasing Hormone (TRH) from the hypothalamus. TRH is stimulated by exercise, stress, malnutrition, low blood glucose and sleep.

Thyroid hormone which is released into blood combines with plasma proteins. Rate of secretion of thyroxine is 90 micrograms/day and rate of secretion of triodothyronine, i.e., T_3 is 5 micrograms/day. Most of the T_4 gets de-iodinated to form T_3, once they enter the peripheral cells. The true intracellular hormone is mainly T_3. T_3 is found freely in the plasma and T_4 is usually bound with plasma proteins. Hence, even at the site of action, T_3 acts faster than T_4.

The level of secretion of TSH depends on the plasma levels of T_3 and T_4, as these hormones affect the sensitivity of the anterior pituitary to TRH. When T_3 and T_4 levels increase, TSH secretion decreases and vice versa.

When iodine supply becomes deficient, excess TSH is secreted and thyroid gland cells proliferate and the thyroid gland enlarges.

3. Regulation of Secretion of Thyroid Gland

The body has a complex mechanism for adjusting the level of thyroid hormones. First, the hypothalamus, located just above the pituitary gland in the brain, secretes a thyrotropin-releasing hormone, which causes the pituitary gland to produce the Thyroid-Stimulating Hormone (TSH). TSH stimulates the thyroid gland to produce thyroid hormones. The pituitary gland slows or speeds the release of TSH, depending on whether the levels of thyroid hormones circulating in the blood are getting too high or too low. This is called the **hypothalamic-pituitary-thyroid axis**.

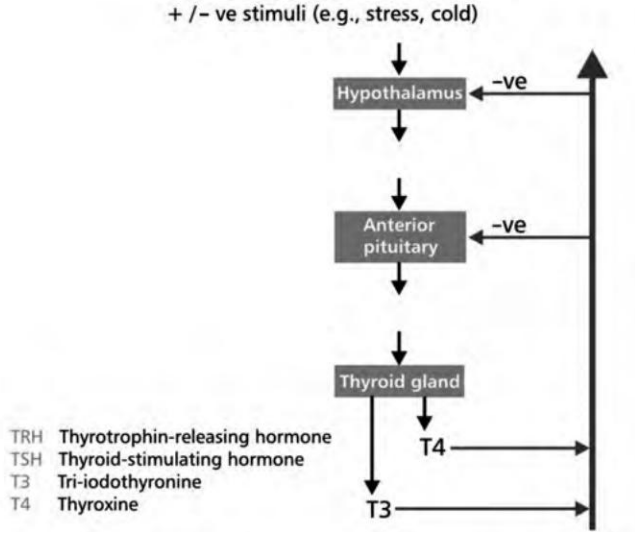


Fig. 12.11 *Thyroid hormone negative feedback loop*

TSH is stimulated by malnutrition, sleep, low plasma glucose, excitement, anxiety and exercise.

The thyroid gland also produces the hormone calcitonin which contributes to bone strength by helping calcium to be incorporated into bone.

4. Functions of the Thyroid Gland

Every cell in the body depends upon thyroid hormones for regulation of their metabolism.

All the functions of the thyroid gland can be summarized under two main actions:

1. To increase the overall metabolic rate in the body
2. To stimulate growth in children

The thyroid plays an important role in regulating the body's metabolism and calcium balance. The T_4 and T_3 hormones stimulate every tissue in the body to produce proteins and increase the amount of oxygen used by cells. The harder the cells work, the harder the organs work. It influences the metabolic rate in two ways—by stimulating almost every tissue in the body to produce proteins and by increasing the amount of oxygen that the cells use. Protein synthesis is increased due to thyroxine. RNA translation is increased and ribosomes are activated which synthesize more proteins.

It helps the body make energy, keep body temperature regulated and assist other organs in their function.

The effect of thyroxine on growth is quite specific. It has an important role to play during fetal life and in infants. It promotes growth.

Red-blood-cell production is increased and erythropoiesis is accelerated.

Thyroid hormones affect many vital body functions, e.g., the heart rate, the respiratory rate, the rate at which calories are burned, immune strength and hormonal balance; the texture and quality of skin and hair, sex drive, fertility, mood elevation and emotional balance.

It promotes development of the brain and increases its blood circulation. It is responsible for the normal functioning of the brain. Increase in thyroxine secretion leads to excessive stimulation of the brain and the person may experience nervousness, anxiety and may develop psychoneurotic problems. Decreased secretion can cause lethargy and somnolence.

Appetite and food intake are increased by thyroxine. It stimulates both, the secretions and motility, of the gastrointestinal tract. So, hypersecretion causes diarrhea and hyposecretion leads to constipation.

It plays an important role in carbohydrate metabolism. It increases glucose absorption from the gastrointestinal tract and accelerates glucose transport across the cell membrane. Glycogen-to-glucose breakdown is increased and it accelerates gluconeogenesis.

It causes mobilization of fat from adipose tissue leading to increase in the free fatty acid level in the blood. It decreases cholesterol and triglyceride level in plasma. Its hyposecretion leads to increased cholesterol levels and this can cause atherosclerosis. Fat deposition in the liver is enhanced and can lead to fatty liver.

It increases enzyme formation. Normal skeletal muscle activity depends, to some extent, on thyroxine. Increase in secretion can cause muscle tremors while decreased secretion leads to sluggishness in muscle contraction and muscle reflexes.

12.3.3 Disorders of the Thyroid Gland

Thyroid function can get disturbed due to thyroid disease itself or due to disorders of the pituitary and/or hypothalamus. When there is deficiency of thyroid-hormone production secondary to insufficient dietary iodine, there is disturbance of thyroid function.

There could be abnormal secretion of thyroid hormones (too much, or too little secretion of T_3 and T_4), or there could be increased growth of the thyroid, causing compression of important neck structures, or it could simply appear as a mass in the neck, or there may be formation of nodules or lumps within the thyroid which could be benign or malignant.

1. Hyperthyroidism

Hyperthyroidism is the term for overactive tissue within the thyroid gland, resulting in overproduction and thus, an excess of circulating free thyroid hormones, thyroxine (T_4), triodothyronine (T_3) or both.

Most of the symptoms are due to increased basal metabolic rate.

The main causes of hyperthyroidism are

1. Graves' disease (the most common etiology in 70–80% of the cases)
2. Toxic thyroid adenoma
3. Toxic multinodular goiter
4. Inflammation of the thyroid, called thyroiditis
5. Oral consumption of excess thyroid hormone tablets
6. Amiodorone, an anti-arrhythmic drug is structurally similar to thyroxine and may cause both under/over activity of the thyroid
7. Postpartum thyroiditis

Hyperthyroidism occurs due to presence of TSH-like substances in the blood. They bind with the same membrane receptors of TSH. They act as antibodies and activate the cycle AMP system of the cell leading to hyperthyroidism. These antibodies are developed due to auto-immunity.

2. Thyrotoxicosis

Graves' disease is an auto-immune disease. The thyroid stimulating auto-antibodies which are produced by the B lymphocytes activate the thyroid stimulating hormone receptors and there is increase in the secretion of the thyroid hormone. There is diffuse swelling of the gland.

Toxic thyroid adenoma is a single, localized tumor in the thyroid gland. The adenoma secretes large quantities of thyroid hormone. It is not associated with auto-immunity. Some patients may develop signs and symptoms of thyrotoxicosis. Some adenomas have a tendency to become malignant in the elderly. When the adenoma is active, the other parts of the thyroid gland will not secrete the thyroid hormone.

Toxic nodular goiter is seen after 40 years of age and is more common in women. There is weight loss with increased appetite, anxiety, intolerance to heat, weakness, hyperactivity, irritability, polyuria, polydipsia, delirium, and excessive

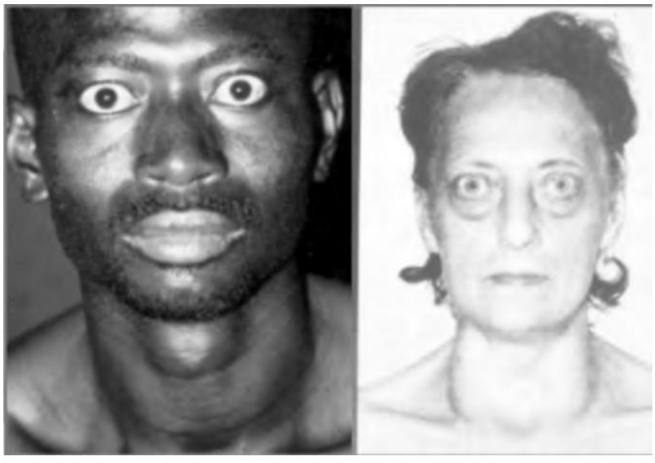


Fig. 12.12 *Exophthalmos—Grave's disease*

sweating. Some have palpitations and arrhythmias, shortness of breath. The thyroid gland is enlarged.

Exophthalmos, i.e., protrusion of the eyeballs is seen. This is due to deposition of fat and fibrous tissue behind the eyes and edematous swelling of the retro-orbital tissues. It is also believed to be part of the auto-immune process. Exophthalmos is mainly seen in Graves' disease.

3. Hypothyroidism

Hypothyroidism occurs when there is insufficient secretion of T_3 and T_4. This is an auto-immune disease. There is inflammation of the gland followed by fibrosis.

Congenital hypothyroidism, or hypothyroidism occurring in infancy or childhood, causes cretinism. In adults, hypothyroidism causes myxoedema.

4. Cretinism

Cretinism is a condition of severely stunted physical growth and mental retardation due to untreated congenital deficiency of thyroid hormones. It could be a genetic disorder, or occur from prolonged nutritional deficiency of iodine. It could be due to insufficient iodine for synthesis of T_3 and T_4, as there is lack of iodine in the diet, especially in hilly areas.

Fig. 12.13 *Cretinism*

There is retarded physical growth; sluggish movements and delayed milestones. If not treated early; the child could become permanently mentally retarded.

In affected children, the face is swollen, and has a dull look. The tongue is big and protruding with an open mouth that drools. The baby is usually listless, slow-moving and a slow feeder.

Abdominal muscle tone is poor and the body appears bloated.

5. Adult Hypothyroidism (Myxedema)

Myxedema is a skin and tissue disorder seen in adults, usually due to severe prolonged hypothyroidism which can be caused by atrophy of the gland, Hashimoto's thyroiditis, severe iodine deficiency, antithyroid drugs or surgical removal of the thyroid gland. It is five times more common in females than males.

There is nonpitting edema. The face is puffy, especially the eyelids.

Fig. 12.14 *Adult woman with the characteristic puffiness that often accompanies hypothyroidism. Her puffiness and hair texture markedly improved after treatment with thyroid*

Generalized fatigue, mental sluggishness and sluggishness of movements, drowsiness and profound lethargy are seen.

There is intolerance to cold. Hoarseness of voice is present and increase in body weight is common.

Decrease in hair growth and hairfall, especially from the lateral part of eyebrows, is seen.

6. Goiter

Goiter is an enlarged thyroid gland. Some people with goiter have an under-active or over-active thyroid. In hypothyroidism, the secretion of the hormones is reduced with enlargement of the gland.

Due to lack of iodine, there is no formation of hormones. Secretion of T_3 and T_4 is reduced and the thyroid swells in

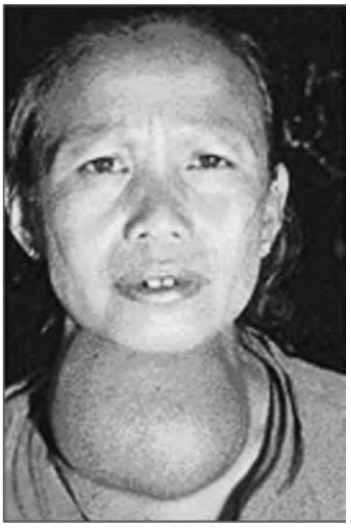


Fig. 12.15 *When the iodine concentration in the blood is low, the thyroid gland enlarges in an attempt to trap as much iodine as possible, sometimes making a visible lump in the neck—a goiter. People with this condition suffer weight gain and sluggishness. In a pregnant woman severe iodine deficiency can cause extreme and irreversible mental and physical retardation of the infant, a condition known as cretinism.*

an attempt to make enough thyroxine and T_3. This results in hyperplasia of the thyroid gland.

In some, there may not be any deficiency of iodine, and still there is enlargement of the thyroid gland. The cause is unknown and it is called **idiopathic nontoxic goiter**.

In this, may be there is deficiency of enzymes required for thyroid-hormone formation.

In many cases there are no symptoms apart from the appearance of a swelling in the neck.

The enlarged thyroid gland can cause pressure symptoms. Pressure on the esophagus could cause dysphagia; tracheal pressure could cause cough and difficulty in breathing and pressure on the recurrent laryngeal nerve can lead to hoarseness of voice.

12.4 PARATHYROID GLANDS

12.4.1 Anatomy

The parathyroid glands are four small endocrine glands in the neck. They are usually located behind the thyroid gland at the upper and lower poles and, in rare cases, within the thyroid gland or in the chest. Each is 6 mm long, 3 mm wide and 2 mm thick. The glands are surrounded by a connective-tissue capsule. They are made up of chief cells and oxyphil cells. Cells are arranged in columns with blood channels between them.

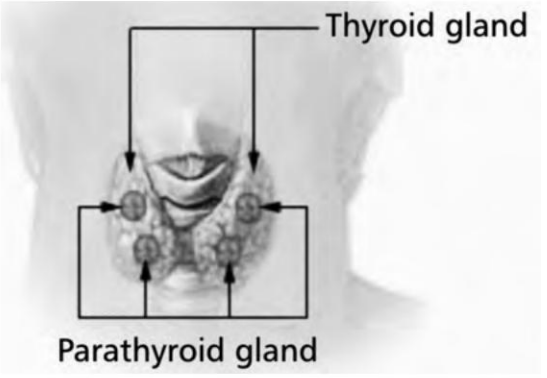


Fig.12.16 *Thyroid and parathyroid glands*

12.4.2 Physiology

1. Hormone

Parathormone (PTH) is secreted by the chief cells. It is proteinic in nature and controls the amount of calcium in the blood and within the bones.

2. Regulation of Parathormone Secretion

When blood-calcium level drops below a certain point, calcium-sensing receptors in the parathyroid glands are activated to release hormone into the blood.

Increase in calcium secretion is seen when there is increased resorption of calcium from the bones, and increase in calcium and /or vitamin D in the diet.

Decrease in calcium in blood is seen in pregnancy, lactation and in rickets.

3. Actions and Functions of Parathormone

The sole function of the parathyroid glands is to maintain the body's calcium level within a very narrow range, so that the nervous and muscular systems can function properly.

It takes part in the control of calcium and phosphate homeostasis, as well as bone physiology. It has effects antagonistic to those of calcitonin. PTH increases blood-calcium levels by stimulating osteoclasts to break down bone and release calcium. It also increases gastrointestinal calcium absorption by activating vitamin D, and promotes calcium uptake by the kidneys.

Parathormone along with calcitonin from the thyroid gland, acts in a complementary manner to maintain blood-calcium level.

12.4.3 Disorders

Decrease in parathormone secretion causes hypocalcaemia and tetany. Increase in parathormone secretion causes hypercalcemia called **hyperparathyroidism**.

1. Hypoparathyroidism

Hypoparathyroidism is a decreased function of the parathyroid glands with decreased levels of parathyroid hormone and hypocalcaemia. This leads to a condition called tetany.

Fig. 12.17 *Tetany*

Tetany is characterized by very strong painful spasms of the skeletal muscles. The most affected muscles are the laryngeal muscles. There is laryngeal spasm and laryngeal stridor which can even result in respiratory arrest and death. Hands show a peculiar attitude called **carpopedal spasm** due to spasm of the hand muscles.

Other symptoms are abdominal pain, generalized pain, convulsions, tingling and numbness, and early cataract.

2. Hyperparathyroidism

Hyperparathyroidism is overactivity of the parathyroid glands resulting in excess production of the parathyroid hormone. It causes high calcium levels (hypercalcemia) and low levels of phosphate in the blood.

There is abdominal pain, gastro-esophageal reflux, anorexia and constipation.

Renal calculi are formed and could be complicated by pyelonephritis and renal failure.

There is general fatigue, muscle weakness and sluggishness of reflex activities.

Osteoporosis is due to excess parathyroid hormone acting directly on the bones causing removal of calcium from the bones.

12.5 ADRENAL GLANDS

12.5.1 Anatomy

The adrenal glands are also known as **suprarenal glands**. They are a pair of star-shaped endocrine glands situated on

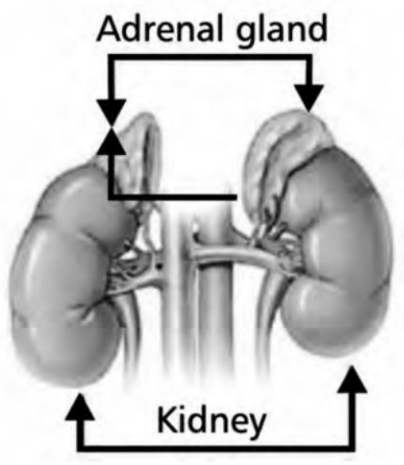


Fig. 12.18 *Location of adrenal glands*

the upper pole of each kidney. They are 4 cm long, 3 cm thick and weigh about 4 grams.

Each gland has two distinct parts which differ in structure and function. The outer part is called the **cortex** and the inner part is called the **medulla**.

The adrenal cortex is composed of three main tissue regions, viz., zona glomerulosa, zona fasciculata, and zona reticularis.

Both receive regulatory input from the system. They are surrounded by adipose capsule and the renal fascia. The adrenal cortex is essential for life.

Adrenal Cortex

The adrenal cortex forms 80% of the adrenal gland. It mediates the stress response through the production of mineralocorticoids and glucocorticoids, namely, aldosterone and cortisol respectively. It is also a secondary site of androgen synthesis.

The adrenal cortex is composed of three main tissue regions:

1. **Zona glomerulosa**, which secretes mineralocorticosteroids—aldosterone.
2. **Zona fasciculata**, which secretes glucocorticosteroids—cortisone, corticosterone, 11-dehydro or 17-hydrocorticosteroids.
3. **Zona reticularis**, which secretes various sex hormones—estrogen, progesterone and androgens.

12.5.2 Physiology

Hormones

The adrenal cortex produces three groups of hormones, collectively known as adrenocortical hormones:

1. **Glucocorticoids**, which regulate carbohydrate metabolism.
2. **Mineralocorticoids**, which regulate the body levels of sodium and potassium.

3. **Androgens** whose actions are similar to that of steroids produced by the male gonads.

1. Adrenocortical Hormones

Synthesis All adrenocortical hormones are steroid in nature and are synthesized from cholesterol which is the major precursor. The basic structure common to all is a steroid ring or cyclopentanoperhydrophenenthrene.

Cholesterol is formed from acetate under the influence of ACTH. It gets converted into pregnenolone. The pathway to pregnenolone synthesis is the same in all zones of the cortex. Pregnenolone moves to the cytosol. After dehydrogenation, it is converted either to 17-hydroxypregnenolone or to 11-deoxycortisol and 11-deoxycorticosterone by enzymes of the endoplasmic reticulum. The latter two compounds then re-enter the mitochondrion, where the enzymes are located for tissue-specific conversion from 11-deoxycortisol to glucocorticoids, cortisol and from 11-deoxycorticosterone to mineralocorticoids (corticosterone) which is converted into aldosterone. From 17- hydroxypregnenolone, the sex hormones androgen and estrogen are formed.

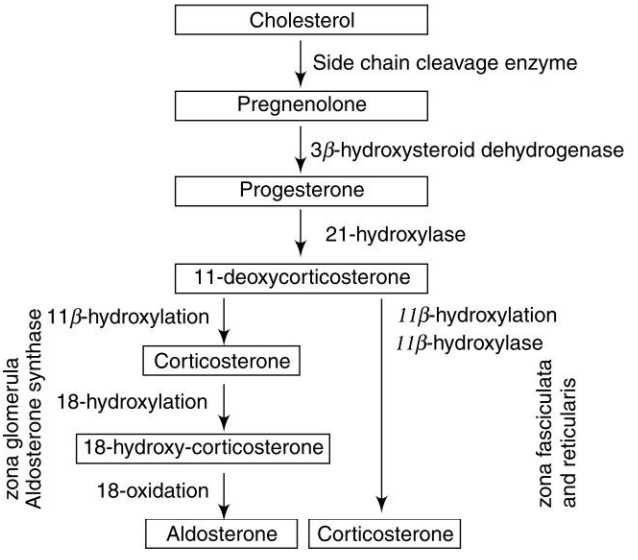


Fig. 12.19 *Enzyme action and location*

Transport and Metabolism Cortisol is transported bound to alpha globulin transcortin. Aldosterone and the sex hormones are found in the blood, bound to albumin. 50% of the aldosterone that is formed is in free form while 50% is in bound form. All are metabolized in the liver. 75% are excreted in urine and 25% in bile and feces.

2. Glucocorticoids

Glucocorticoids (GC) are a class of steroid hormones which bind to the glucocorticoid receptor, which is present in almost every cell.

The main glucocorticoids are cortisol, corticosterone and cortisone. Cortisol (hydrocortisone) is the most important glucocorticoid. It is essential for life and regulates a variety of important cardiovascular, metabolic, immunologic, and homeostatic functions. It helps to withstand stress and trauma in life.

(a) Regulation of Glucocorticoid Secretion Glucocorticoid secretion is stimulated by ACTH from the anterior pituitary and by stress.

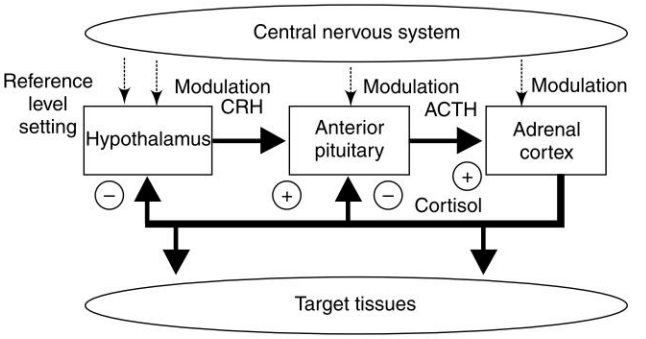


Fig. 12.20 *Structure diagram of the HPA axis*

In nonstressful situations, secretion is influenced by the circadian rhythm.

The highest level of the hormone is between 4 a.m. and 8 a.m. and the lowest level is between 12.00 a.m and 3 a.m.

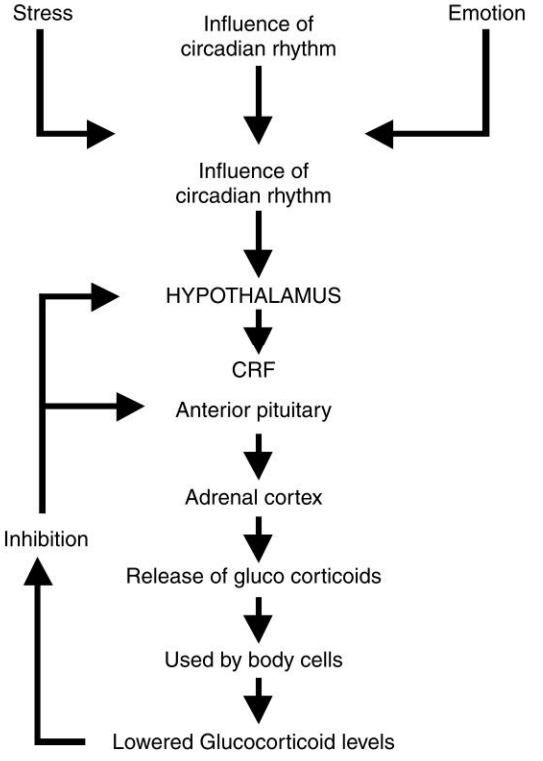


Fig. 12.21 *Regulation of glucocorticoid secretion*

When there is stress, the hypothalamus is stimulated and a corticotrophin-releasing hormone is secreted which acts on the anterior pituitary, and ACTH is released. This causes release of glucocorticoids from the adrenal cortex and its level is raised in blood. This is used by the body cells and the blood glucocorticoid level falls.

Increased blood glucocorticoid level inhibit release of corticotrophin-releasing hormone from hypothalamus and ACTH from the anterior pituitary. So cortisol secretion is inhibited.

(b) Physiological and Pharmacological Actions of Glucocorticoids Glucocorticoids have widespread effects.

(i) Effect on Carbohydrates

- The principle effect of glucocorticoids is on carbohydrates and hence the name.
- They stimulate several processes that collectively serve to increase and maintain normal concentrations of glucose in blood.
- They stimulate gluconeogenesis in the liver and formation of glycogen.
- They mobilize amino acids from extrahepatic tissues, and these serve as substrates for gluconeogenesis.
- They inhibit glucose uptake and its oxidation in muscle and adipose tissue: a mechanism to conserve glucose.
- They help in absorption of sugar from the intestine and from renal tubules.

(ii) Protein Metabolism Protein breakdown is stimulated, releasing amino acids, which are transported into liver cells and are used for synthesis of other proteins, e.g., enzymes, plasma proteins and for gluconeogenesis. There is loss of body proteins and increase in nitrogen secretion. Protein synthesis is also decreased by interfering with nucleic-acid metabolism. This results in muscle wasting, increase in the excretion of uric acid and creatinine in urine, osteoporosis and dissociation of lymphoid tissue.

(iii) Fat Metabolism Stimulation of fat breakdown takes place in adipose tissue: the fatty acids are released by lipolysis and are used for production of energy in tissues like muscle, and the released glycerol provide another substrate for gluconeogenesis. They stimulate fat absorption from the intestine. They mobilize fat from the tissues and disintegrate it in the liver to form ketone bodies. They depress synthesis of fat from carbohydrates.

(iv) Blood Glucocorticoids decrease the number of circulating eosinophils and lymphocytes by increasing their destruction. Hence, there is eosinopenia and lymphopenia. They can cause involution of thymus, spleen, lymph glands, etc.

(v) Effect on Other Metabolism Glucocorticoids have a weak mineralocorticoid effect. There is promotion in the absorption of sodium and water from renal tubules. They also increase retention of calcium and increase excretion of potassium. The basal metabolic rate is stimulated. They play an important role in the maintenance of water balance.

(vi) Anti-inflammatory and Immunosuppressive Properties Whenever there is tissue injury, there is cellular response. Glucocorticoids prevent the inflammatory changes in the cells that occur following cell injury or infection (healing is delayed). They decrease migration of leucocytes into the area of injury.

(vii) Effect on Cardiovascular System They play some role in maintaining blood pressure. Hence, in deficiency of adrenal cortex, there is hypotension.

(viii) Effect on Nervous System Glucocorticoids are essential for normal functioning of the nervous system.

(ix) Miscellaneous Effects Whenever there is any sort of stress, whether physical or mental, there is excessive secretion of ACTH. This increases glucocorticoid level in the blood, which is necessary for survival, as it increases the resistance of the body to stress.

Excessive glucocorticoid levels resulting from administration of a drug or hyperadrenocorticism have effects on many systems. There is inhibition of bone formation, suppression of calcium absorption and delayed wound healing.

3. Mineralocorticoids

The primary endogenous mineralocorticoid is aldosterone, although a number of other endogenous hormones (including progesterone and deoxycorticosterone) have mineralocorticoid function. It is very essential for life and is called the life-saving hormone.

(a) Regulation of Secretion The two most significant regulators of aldosterone secretion are

- **Concentration of potassium ions in extracellular fluid**—small increases in blood levels of potassium strongly stimulate aldosterone secretion.
- **Angiotensin II**—Activation of the renin-angiotensin system as a result of decreased renal blood flow (usually due to decreased vascular volume).

Decrease in sodium-ion concentration and extracellular fluid volume stimulate secretion of aldosterone through the renin–angiotensin–aldosterone system.

Renin is secreted when sodium level falls or there is decrease in renal blood flow. It converts angiotensinogen into angiotensin I which is converted into angiotensin II by the enzymes in the lungs. This stimulates secretion of aldosterone. There is retention of sodium and water which causes increase in ion concentration and increase in extracellular fluid volume. There is thus, an inhibitory feedback mechanism. Renin

release is then stopped and the secretion of aldosterone from the adrenal cortex ceases.

(b) Physiological Actions

1. The main action of aldosterone is to maintain water and electrolyte balance in the body. Aldosterone acts on the kidney promoting the reabsorption of sodium ions (Na+) into the blood. Water follows the salt and this helps maintain normal blood pressure.
2. When the blood pressure is elevated due to increase in blood volume, there is pressure diuresis. Water and salt excretion in urine is greatly increased. Concentration of sodium and water comes down in blood. Actually, this is a secondary effect of pressure diuresis and hence is called aldosterone escape. Water and salt content become normal.
3. Aldosterone increases potassium excretion and so in deficiency of aldosterone secretion, hyperkalemia could develop which can cause cardiac arrhythmias and weak cardiac contractions. Increase in aldosterone secretion can cause hypokalemia and muscle weakness.
4. Aldosterone is essential to maintain acid–base balance of the body. Hyposecretion causes acidosis and hypersecretion causes alkalosis.
5. *Miscellaneous effects*
   (a) It increases sodium reabsorption in the colon.
   (b) It increases reabsorption of sodium in the salivary glands.
   (c) It acts on sweat glands to reduce the loss of sodium.
   (d) It acts on taste cells to increase the sensitivity of the taste buds to sources of sodium.

4. Sex Hormones

The adrenal cortex secretes precursors to androgens such as testosterone, while a small amount of estrogen and progesterone are also secreted.

In sexually mature males, this source is so much lower than that of the testes that it is probably of little physiological significance. Their exact role is not very clear; however, excessive production of adrenal androgens can cause premature puberty in young boys. In females, the adrenal cortex is a major source of androgens. Their hypersecretion may produce a masculine pattern of body hair and cessation of menstruation.

12.5.3 Disorders of the Adrenal Cortex

1. Cushing's Syndrome

Cushing's syndrome is an endocrine disorder caused by high levels of cortisol in the blood. This can be caused by tumors of the adrenal gland that produce cortisol or Adrenocorticotropic Hormone (ACTH) or malignant tumors of non-endocrine origin, e.g., bronchogenic carcinoma which secretes ACTH. This disease can also be caused by prolonged glucocorticoid drug therapy. Hypothalamic disorder causing excess of CRF secretion can lead to increased secretion of ACTH. An adenoma in the pituitary gland that produces large amounts of ACTH, which in turn elevates cortisol, can lead to Cushing's syndrome.

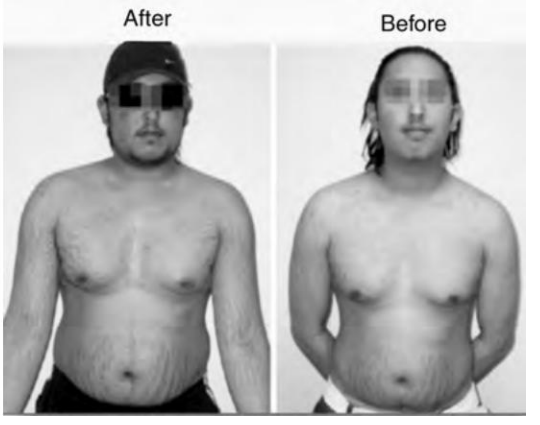


Fig. 12.22 *Cushing's syndrome*

There is gain in weight. The face becomes rounded and is often referred to as 'moon face'. There is thinning of the skin which causes easy bruising and dryness, particularly over the hands and other mucous membranes. Hyperglycemia occurs due to excessive gluconeogenesis. There is depression of the immune and inflammatory responses leading to infection. There is osteoporosis. CNS symptoms in the form of excitability, insomnia, psychosis, depression are seen. There may be hirsutism (male-pattern hair growth in a female) and oligomenorrhea due to elevation in androgen levels.

2. Hyperaldosteronism

Hyperaldosteronism is a condition where there is overproduction of aldosterone leading to fluid retention and increased blood pressure, weakness, and, rarely, periods of paralysis.

Depending on the causes, hyperaldosteronism is of two types:

(a) Primary hyperaldosteronism
(b) Secondary hyperaldosteronism

(a) Primary Hyperaldosteronism Primary hyperaldosteronism is caused by a tumor of the adrenal gland. There is excessive secretion of mineralocorticoids.

(b) Secondary Hyperaldosteronism Secondary hyperaldosteronism occurs when there is low renal perfusion, e.g., congestive cardiac failure or low levels of serum sodium.

High aldosterone levels can lead to low potassium levels which often produce no symptoms but may lead to weakness, tingling, muscle cramps, and periods of temporary paralysis. There may be polyuria and polydipsia.

Hypertension is recorded and there may be metabolic acidosis.

3. Adrenogenital Syndrome

This condition is also known as congenital adrenal hyperplasia.

It is an autosomal recessive disorder of steroid-hormone production in the adrenal glands, leading to a deficiency of cortisol. The pituitary gland responds by secreting massive amounts of the stimulating hormone corticotropin to bring the cortisol levels up to normal. This hormone, in turn, causes the adrenal glands to overproduce certain intermediary hormones which have testosterone-like effects on the fetus and the child, leading to virilization.

Secondary sexual characters develop in the female. This is called **adrenal virilism**. There is increased muscular growth and male distribution of hair. Amenorrhea and enlargement of clitoris is seen in females. Also, the voice deepens as in males.

4. Addison's Disease

Addison's disease occurs when the adrenal glands do not produce enough of the hormone cortisol and, in some cases, the hormone aldosterone. The disease is also called adrenal insufficiency, or hypocortisolism.

It may be due to a disorder of the adrenal glands themselves (primary adrenal insufficiency) or due to inadequate secretion of ACTH by the pituitary gland (secondary adrenal insufficiency).

5. Primary Adrenal Insufficiency

There is gradual destruction of the adrenal cortex, the outer layer of the adrenal glands, by the body's own immune system. About 70 per cent of Addison's disease is caused by autoimmune disorders, in which the immune system makes antibodies that attack the body's own tissues or organs and slowly destroy them. Adrenal insufficiency occurs when at least 90 per cent of the adrenal cortex has been destroyed. Both glucocorticoid (cortisol) and mineralocorticoid hormones are lacking.

6. Secondary Adrenal Insufficiency

It is more common than primary adrenal insufficiency and is due to a lack of ACTH. The adrenal gland's production of cortisol drops. A temporary form of secondary adrenal insufficiency may occur when a person who has been receiving a glucocorticoid hormone such as prednisone for a long time abruptly stops taking the medication. Glucocorticoid hormones block the release of both corticotropin-releasing hormone (CRH) and ACTH. Normally, CRH instructs the pituitary gland to release ACTH. If CRH levels drop, the pituitary is not stimulated to release ACTH, and the adrenals then fail to secrete sufficient levels of cortisol.

Another cause of secondary adrenal insufficiency is the surgical removal of benign, or noncancerous, ACTH-producing tumors of the pituitary gland where the source of ACTH is suddenly removed. Tuberculosis of the adrenal glands can also produce this disease.

There is muscle weakness, lethargy, tiredness, mental confusion and weight loss. There may be hypotension and hypoglycemia. Increased pigmentation of the skin and mucous membranes may occur. Susceptibility to infection increases.

7. Addisonian Crisis

Addisonian crisis is also known as acute adrenal cortical insufficiency.

Whenever a person with chronic adrenal cortex insufficiency is exposed to stress in the form of surgical operation, acute infection, trauma or there is sudden withdrawal of steroids in a patient who is on prolonged therapy, this syndrome is seen.

There is severe nausea, vomiting and diarrhea; electrolyte imbalance and hypotension followed by sudden circulatory collapse.

12.5.4 Adrenal Medulla

1. Physiology

The adrenal medulla is part of the adrenal gland. It is located at the center of the gland, being surrounded by the adrenal cortex. It forms 20% of the adrenal gland. The adrenal medulla consists of irregularly shaped cells grouped around blood vessels. These cells are intimately connected with the sympathetic division of the autonomic nervous system. They are modified postganglionic neurons, and preganglionic autonomic nerve fibers come from the central nervous system.

The adrenal medullary hormones are called catecholamines as they are amines and derivatives of catechol. The most abundant catecholamines are epinephrine (adrenaline), norepinephrine (noradrenaline) and dopamine, all of which are produced from phenylalanine and tyrosine.

2. Regulation of Secretion of Adrenaline and Noradrenaline

Normally, adrenaline and noradrenaline are secreted by the adrenal medulla. When the body is under stress, large amount of catecholamines are secreted to maintain the disturbed homeostasis.

The response to stress is of two types:

1. Immediate response
2. Longer response

During immediate response, the sympathetic part of the autonomic nervous system is stimulated. So adrenaline and noradrenaline are released which give rise to increase in heart rate, increase in metabolic rate, increase in blood pressure and dilation of pupils. Blood is diverted to essential organs like the brain, heart and skeletal muscles by dilating their blood vessels. This is called fight-or-flight response.

In the longer response, ACTH from the anterior pituitary stimulates the release of glucocorticoids and mineralocorticoids from the adrenal cortex and a prolonged response to stress occurs.

Stress could be in the form of fright, exercise, infection, disease, fasting, hypoglycemia, exposure to cold and emotional disturbances.

3. Actions of Adrenaline and Noradrenaline

Adrenaline and noradrenaline have the same effect as that of sympathetic stimulation.

1. Adrenaline increases oxygen consumption and carbon-dioxide removal in the tissues.
2. Blood-glucose level increases under the influence of adrenaline at tissue level.
3. Free fatty acids are mobilized from adipose tissue.
4. Adrenaline reduces blood-coagulation time.
5. Adrenaline increases the force of contraction of the heart and increases heart rate.
6. Adrenaline increases systolic blood pressure by increasing cardiac output and force of contraction and decreases diastolic blood pressure by decreasing peripheral resistance.

   The effect on blood pressure is more by noradrenaline as compared to adrenaline because noradrenaline causes vasoconstriction of the blood vessels throughout the body. There is increase in total peripheral resistance, and diastolic blood pressure also increases.
7. Rate and force of respiration is increased by adrenaline. It also causes bronchodilatation.
8. Adrenaline increases the activity of the brain.
9. Adrenaline has a strong effect on the skeletal muscles. It causes powerful contraction which leads to fatigue of the muscles. Glycogenolysis is increased and glucose is released from the muscle into the blood.

   Dopamine, which is secreted from the adrenal medulla, is also secreted from some cells in the brain where it acts as a neuro-transmitter.

4. Disorders

The main disorders seen in adrenal medulla are tumors which are hormone secreting.

There are two types of tumors:

1. Benign : Pheochromocytoma
2. Malignant : Neuroblastoma

(a) Pheochromocytoma Pheochromocytoma is a benign neuroendocrine tumor of the medulla of the adrenal glands originating in the chromaffin cells. It may occur in one or both the glands. There is excessive secretion of catecholamines.

The signs and symptoms of pheochromocytoma are those of sympathetic nervous system hyperactivity. There is tachycardia, hypertension, palpitation, headache, pallor, anxiety, weight loss and hyperglycemia with glycosuria. Hypertension is paroxysmal. Orthostatic hypotension is common.

(b) Neuroblastoma Neuroblastoma is a malignant tumor seen in infants and children. It is a neuroendocrine tumor, arising from any neural crest element of the sympathetic nervous system. The cause of neuroblastoma is unknown, though many believe that it is an accidental cell growth that occurs during normal development of the adrenal glands. It is known to undergo spontaneous regression.

12.6 THYMUS

12.6.1 Anatomy

The thymus gland is situated in the upper anterior portion of the chest cavity (mediastinum) behind the sternum, in front of the trachea. It lies below the thyroid gland and extends a little into the root of the neck.

It is of a pinkish-gray color, soft, and lobulated on its surfaces. It is small at birth and it enlarges during childhood, and atrophies at puberty. It reaches its maximum weight (20 to 37 grams) by the time of puberty. It remains active only until puberty. As one ages, the thymus slowly shrinks, eventually degenerating into tiny islands of fatty tissue.

It has two lobes enclosed in a fibrous capsule. The lobes are joined by areolar tissue. The fibrous capsule goes into the substance of the gland, dividing it into lobules. The gland has lymphocytes and epithelial cells.

The thymus differs structurally from other lymphoid organs as it does not have lymphatic vessels draining into it. It is not a filter like the lymph nodes.

12.6.2 Physiology

The main function of the thymus is to provide an area for T-lymphocyte maturation. The thymus also helps protect against auto-immunity.

The thymus gland has two functions:

1. Lymphoid function
2. Endocrine function

1. Lymphoid Function

The thymus plays an important role in the development of immunity. During fetal development and childhood, the thymus

is involved in the production and maturation of T-lymphocytes, a type of white blood cell important in the immune system. Lymphocytes originate in the red bone marrow. When they enter the thymus, they are processed into T-lymphocytes which travel to the lymph nodes and also enter the blood. There they help the immune system protect the body from viruses, fungus, and other types of infections.

2. Endocrine Function

Two hormones are secreted from the thymus gland, viz., thymosin and thymin.

Thymosin is secreted by the epithelial cells of the gland and the main function is to promote the proliferation of T-lymphocytes.

Thymin, also known as **thymopoietin**, is also secreted from the thymus and its main action is to inhibit acetylcholine release and thus suppression of neuromuscular activity.

When there is hyperactivity of thymus, it causes a disease called **Myaesthenia gravis**. Usually in these people, the thymus gland has to be removed as a part of treatment.

12.7 PINEAL BODY (EPIPHYSIS)

The pineal body is a small endocrine gland. It produces melatonin, a hormone that affects the modulation of wake/sleep patterns and photoperiodic (seasonal) functions. It is shaped like a tiny pine cone (hence its name), and is located near the center of the brain, between the two hemispheres, in a groove where the two rounded thalamic bodies join.

It is attached to the roof of the third ventricle by a short stalk. It lies above the hypothalamus and is connected to it through nerves which form the stalk.

It is surrounded by a capsule and is reddish brown in color.

It has two types of cells:

1. Parenchymal cells
2. Neuroglial cells

The hormone secreted by the parenchymal cells is melatonin. Secretion of melatonin is controlled by the amount of light entering the eyes. It is secreted more in darkness and at night and less during daytime.

The significance of neuroglial cells is not clear.

Functions

1. The role of the pineal gland in human beings is not very clear, especially the sexual functions. In animals, melatonin stimulates the gonads and regulates seasonal fertility.

   It inhibits growth and development of sex organs before puberty.

2. Probably it controls different activities during different times of the day. This is called **circadian rhythm**. This control is influenced by the hypothalamus.

The pineal gland atrophies after puberty and in the adult, may be calcified.

12.8 PANCREAS

12.8.1 Anatomy

The pancreas is a gland–organ in the digestive and endocrine system. It is situated in the abdominal cavity, is 12 to 15 cm long and has three parts, namely head, body and tail. It is both an endocrine gland producing several important hormones, including insulin, glucagon, and somatostatin, as well as an exocrine gland, secreting pancreatic juice, containing digestive enzymes that pass to the small intestine. These enzymes help in the further breakdown of the carbohydrates, protein, and fat in the chyme.

The part of the pancreas with endocrine function is made up of a million cell clusters called the **islets of Langerhans**. They are ductless glands and the hormones which are secreted from these glands directly enter the blood to circulate in the body. There are four types of cells in the islets. They are relatively difficult to distinguish using standard staining techniques, but they can be classified by their type of secretion.

12.8.2 Physiology

1. α cells, also called A cells, secrete glucagon.
2. β cells, or B cells, secrete insulin.
3. δ cells, or C cells, secrete somatostatin.
4. PP cells, or D cells, secrete pancreatic polypeptide.

The capillaries of the islets are lined by layers of endocrine cells in direct contact with the vessels, and most endocrine cells are in direct contact with blood vessels by either cytoplasmic processes or by direct apposition.

The main hormones are insulin and glucagon and both are secreted in response to blood-sugar levels but have opposite actions. (See Fig. 12.23)

1. Insulin

Insulin is a peptide hormone composed of 51 amino acids, arranged in two chains—the B and A chains—which are bound together by disulphide bonds. Chain A contains 21 amino acids and Chain B contains 30 amino acids.

Insulin circulates in the blood, bound to a β-globulin, and is inactivated by an enzyme gluthathion insulin transhydrogenase.

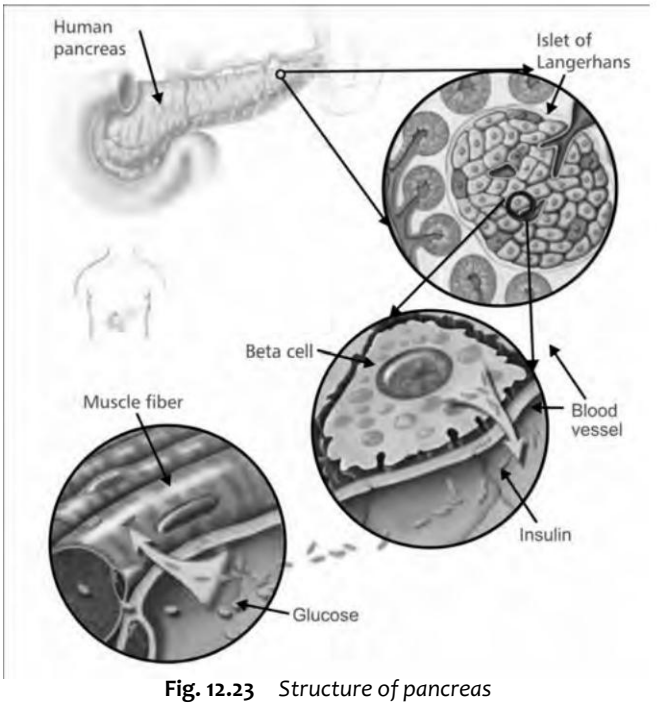


Fig. 12.23 *Structure of pancreas*

(a) Physiological Actions of Insulin Insulin is a hormone with extensive effects on body metabolism.

The main action of insulin is to regulate **carbohydrate** metabolism. It causes most of the body's cells to take up glucose from the blood (including liver, muscle, and fat tissue cells), storing it as glycogen in the liver and muscle. It stops use of fat as an energy source. It also prevents breakdown of glycogen into glucose in muscles and the liver.

It increases **protein** synthesis. Uptake of amino acids by the cells is accelerated and catabolism of proteins is inhibited. Also, the release of amino acids from the cells is decreased. Thus, it prevents the formation of glucose from proteins. Insulin promotes storage of proteins and indirectly promotes growth of the body.

It promotes synthesis of **fat** and storage of fat in the adipose tissue. The excess glucose in the cells is used for synthesis of fatty acids by activating enzymes.

When insulin is absent (or low), glucose is not taken up by most of the body cells. Therefore, the body begins to use fat as an energy source and lipids are transferred from adipose tissue to the liver.

(b) Regulation of Insulin Secretion The stimulus for insulin secretion is high blood glucose. The amount of insulin secreted into the blood increases as the blood glucose rises. Similarly, as blood glucose falls, the amount of insulin secreted by the pancreatic islets goes down.

Insulin has an effect on a number of cells, including muscle cells, red blood cells, and fat cells. In response to insulin, these cells absorb glucose from the blood, bringing the high blood-glucose levels into the normal range.

[Refer to the chapter on cell to see an algorhythmic chart about the homeostasis of blood-glucose level.]

There are also other factors controlling insulin secretion.

When amino-acid level in the blood rises, it stimulates insulin secretion. This action is better carried out when blood-glucose level is also increased. The two are contributory to each another. Amino acids, too, increase the action of glucose on insulin secretion.

Gastrointestinal secretions like gastrin, secretin and cholecystokinin increase insulin secretion.

Insulin secretion is decreased by glucagon, cortisol, adrenaline and somatostatin.

Sympathetic stimulation decreases and parasympathetic stimulation increases insulin secretion.

(c) Regulation of Blood-Glucose Level The blood-sugar concentration or blood-glucose level is the amount of glucose present in the blood. It is absolutely essential that blood-glucose levels are properly regulated, as it is the main nutrient utilized by tissues and it is the primary source of energy for the body's cells.

Glucose molecules are broken down within cells, in order to produce Adenosine Triphosphate (ATP) molecules—energy-rich molecules that power numerous cellular processes. Glucose molecules are delivered to cells by the circulating blood; and, therefore, to ensure a constant supply of glucose to cells, it is essential that blood-glucose levels be maintained at relatively constant levels.

Blood-glucose concentration is maintained within the normal range of 70 to 110 milligrams of glucose per deciliter of blood, by negative feedback mechanism.

Major factors that can increase blood-glucose levels are glucose absorption by the small intestine (after ingesting a meal), 'stress' hormones such as adrenaline, several of the steroids, infections, trauma and the production of new glucose molecules by liver cells.

Major factors that can decrease blood-glucose levels are the transport of glucose into cells and the loss of glucose in urine.

When levels of blood sugar rise, insulin is released from beta cells of the islets of Langerhans in the pancreas. The liver converts more glucose into glycogen (glycogenesis), and some of the body's cells, primarily muscle and fat tissue cells, take up glucose from the blood through the GLUT4 transporter, thus decreasing blood sugar.

If blood-glucose levels fall below normal levels (during the post-absorptive or fasting state, or during starvation or during very heavy exercise), insulin secretion is inhibited and, at the same time, the alpha cells of the pancreas release glucagon, which has the following actions:

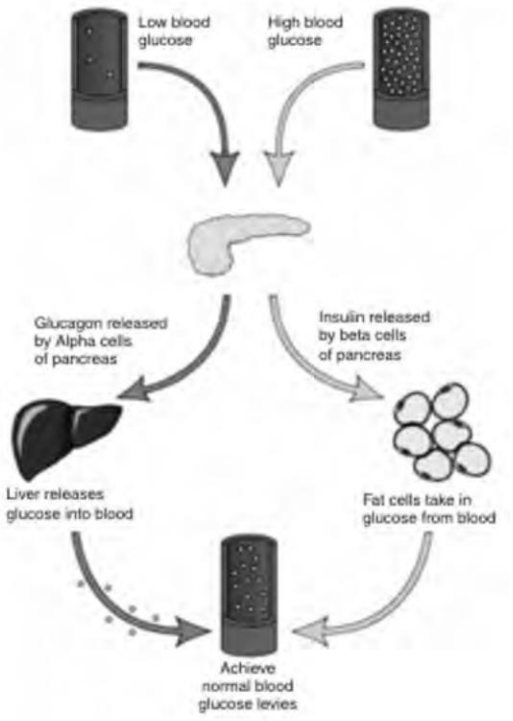


Fig. 12.24 *Regulation of blood-glucose level (Refer colour figure)*

1. It accelerates the breakdown of glycogen to glucose in liver and skeletal muscle cells (glycogenolysis). The glucose is released into the bloodstream, increasing blood-sugar levels.
2. It increases the breakdown of fats to fatty acids and glycerol in adipose tissue and releases them into the blood, which cells can use for energy.
3. It stimulates liver cells to increase glucose synthesis (from glycerol absorbed from the blood) and release glucose into the blood.

These effects collectively cause an increase in blood-glucose levels and thus glucose level returns to normal.

Besides insulin and glucagon, there are other hormones that can influence blood-glucose levels. The most important ones are epinephrine, cortisol, thyroxine and growth hormone, all of which can increase blood-glucose levels.

(a) Epinephrine It increases blood-glucose level by increasing glycogenolysis in liver and muscle.

(b) Cortisol It increases blood-glucose level by increasing gluconeogenesis in liver from amino acids. Protein breakdown is also increased, mainly in the muscle cells. Glucose uptake and glucose utilization by the peripheral cells is reduced. Thus, glucose level is increased.

(c) Thyroxine It increases absorption of glucose from the gastro-intestinal tract and breakdown of glycogen to glucose is also increased. Gluconeogenesis is increased.

(d) Growth Hormone It increases blood-glucose levels. Peripheral utilization of glucose is reduced. It increases conversion of glucose into glycogen in the cells. After some time, the cells get saturated with glycogen and glucose cannot enter the cells. The overall effect is an increase in the blood-glucose level.

2. Glucagon

Glucagon is secreted by the alpha cells of the pancreatic islets in much the same manner as insulin, except that it is in the opposite direction. If blood glucose is high, then no glucagon is secreted. When blood glucose goes low, e.g., between meals and during exercise, more and more glucagon is secreted. Like insulin, glucagon has an effect on many cells of the body, but most notably on the cells of the liver. The effect of glucagon is to make the liver release the glucose, which has been stored in its cells, into the bloodstream, with the net effect of increasing blood glucose.

It increases the release of free fatty acids from adipose tissue and these free fatty acids are utilized peripherally.

It inhibits gastric secretion and increases the secretion of bile.

Glucagon promotes formation of glucose from the proteins in the liver.

Regulation of Glucagon Secretion The main stimulus for secretion of glucagon is a low blood-glucose level. In hypoglycemia, more glucagon is released. When there is hyperglycemia, glucagon secretion is decreased.

Glucagon secretion is also stimulated during exercise. Also, increase in amino-acid level stimulates glucagon secretion.

During stressful conditions, glucagon secretion increases. Gastrin, cholecystokinin and cortisol stimulate glucagon secretion.

There are certain situations which inhibit glucagon secretion, e.g., insulin, somatostatin, ketones and free fatty acids.

3. Somatostatin

Somatostatin inhibits the secretion of both insulin and glucagon by acting on the islets of Langerhans.

It inhibits gastric secretion and reduces the motility of stomach, duodenum and the gall bladder.

Its secretion is stimulated by raised glucose level, increase in amino acids and cholecystokinin.

12.8.3 Disorders of Pancreas

1. Diabetes Mellitus (DM)

Diabetes mellitus is a chronic disease associated with abnormally high levels of the sugar/glucose in the blood, characterized by deranged secretion of insulin and/or glucagon with disturbances of carbohydrate, protein and lipid metabolism.

Diabetes is of two types, viz., juvenile (right from birth) and maturity onset. The signs and symptoms of both types of diabetes include fatigue, increased urine output, increased thirst and increased appetite. Diabetes is diagnosed by blood-glucose testing, the glucose-tolerance test, and testing of the level of glycosylated hemoglobin (glycohemoglobin or hemoglobin A1C). The mode of treatment depends on the type of the diabetes.

Pathophysiology It is either due to insufficient production of insulin, or production of defective insulin, or the body cells do not use insulin properly or do not respond appropriately even when insulin is present (inadequate sensitivity of cells to the action of insulin), which leads to hyperglycemia and diabetes.

The latter condition affects mostly the cells of muscle and fat tissues, and results in a condition known as insulin resistance.

There are two main types of diabetes which correspond to two mechanisms and are called insulin dependent (type 1) and non-insulin dependent (type 2) diabetes.

In **type 1 diabetes**, there is no insulin or not enough of it. The body fails to produce insulin, usually, secondary to a destructive process affecting the insulin-producing beta cells in the pancreas. Hence, the pancreas make little or no insulin. Type 1 diabetes usually occurs in children and young adults. Their diabetes can be controlled with injectable insulin only.

In **type 2 diabetes**, there is generally enough insulin but there is insulin resistance, a condition in which cells fail to use insulin properly. It is the most common form of diabetes. It appears in middle-aged adults.

If there is resistance to insulin, the body can, to some degree, increase production of insulin and overcome the level of resistance. After some time, if production decreases and insulin cannot be released enough, hyperglycemia develops. There is also a steady decline of beta-cell function that adds to the process of elevated blood sugar.

Both forms of diabetes may be inherited. A family history of diabetes can significantly increase the risk of developing diabetes.

Other Factors which can cause Diabetes

- Increased hepatic glucose production (e.g., from glycogen to glucose conversion)
- Decreased insulin-mediated glucose transport in muscle and adipose tissues (receptor and post-receptor defects)
- Impaired beta-cell function—loss of early phase of insulin release in response to hyperglycemic stimuli

2. Other Forms of Diabetes

Impaired Glucose Tolerance (IGT) It is a pre-diabetic state of dysglycemia (two-hour glucose levels of 140 to 199 mg per dL, fasting glucose levels of 100 to 125 mg per dL) that is associated with insulin resistance and increased risk of cardiovascular pathology. In prediabetes, blood-sugar levels are higher than normal, but not considered high enough to qualify as Type 2 diabetes. Prediabetes is however, a risk factor for the development of Type 2 diabetes, and thus people affected are an important target group for primary prevention.

Gestational Diabetes It is seen during pregnancy. Here, glucose intolerance is transitory. Even though it may be transient, untreated gestational diabetes can damage the health of the fetus or mother.

- Diabetes is also seen with other conditions like Cushing's syndrome or pheochromocytoma.
- Stress can also induce diabetes.

Symptoms and Signs The classical symptoms of DM are polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger). There may be fatigue, loss of weight, pruritus, infections like tuberculosis, carbuncles, urinary infections and impotence.

Complications Untreated diabetes can lead to many serious medical problems like blindness (retinopathy), kidney disease, CardioVascular Disease (CVD), hypertension, cardiomyopathy, neuropathy and ulceration and gangrene of the feet.

3. Hypoglycemia

Hypoglycemia or low blood sugar occurs when blood sugar level falls below 50 mg/dl.

When blood glucose falls, glucagon signals the liver to break down glycogen and release glucose into the bloodstream. Blood glucose will then rise toward a normal level. In some people with diabetes, this glucagon response to hypoglycemia is impaired and other hormones such as epinephrine may raise the blood-glucose level. But with diabetes treated with insulin or pills that increase insulin production, glucose levels can't easily return to the normal range.

Hypoglycemia can happen suddenly. It is usually mild and can be treated quickly and easily by eating or drinking a small amount of glucose-rich food. If left untreated, hypoglycemia can get worse and cause confusion, clumsiness, or fainting. Severe hypoglycemia can lead to seizures, coma, and even death.

REVIEW QUESTIONS

1. Describe the types of hormones. How is the secretion of hormones controlled? What is the mechanism of action of hormones?
2. Describe the anatomy of the anterior pituitary. Explain the physiology of hormones of the anterior pituitary
3. Explain the anatomy and physiology of the posterior pituitary.
4. Classify disorders of the pituitary gland and explain them briefly.
5. Discuss synthesis, functions and regulation of the thyroid hormone.
6. Discuss various disorders of the thyroid gland.
7. Describe the anatomy and physiology of the parathyroid gland. Write a note on hypoparathyroidism and hyperparathyroidism.
8. Describe synthesis and metabolism of adrenocortical hormones.
9. Describe regulation of glucocorticoids and mineralocorticoids and their actions.
10. Describe regulation of hormones of adrenal medulla and their actions. Write a note on pheochromocytoma and neuroblastoma.
11. Describe the role of pancreas as an endocrine gland.
12. Write short notes on:
    a. Sex hormones
    b. Pineal body
    c. Thymus
    d. Growth hormone
    e. TSH
    f. ACTH
    g. Prolactin
    h. ADH
    i. Oxytocin
    j. Pituitary dwarfism
    k. Diabetes insipidus
    l. Functions of the thyroid gland
    m. Glucocorticoids
    n. Mineralocorticoids
    o. Hyperaldosteronism
    p. Insulin and blood-glucose level regulation
    q. Glucagon
    r. Diabetes mellitus

Chapter

13 Excretory System

- **KIDNEYS**
  - **Anatomy**
    - Organs related to kidneys
    - Structure of the kidney
    - Macroscopic
      - Cortex
      - Medulla
      - Renal sinus
      - Arterial supply, venous drainage,
      - Lymphatic drainage, nerve supply
    - Microscopic
      - Nephron
        - Bowman's capsule
        - Proximal convoluted tubule
        - Loop of Henle
        - Distal convoluted tubule
      - Histology
      - Glomerulus
      - Juxtaglomerular apparatus
    - Functions of the kidney
  - **Physiology**
    - Physiology of urine formation
      - Glomerular filtration
      - Selective reabsorption
        - Active transport
        - Passive reabsorption
      - Tubular secretion
    - Counter-current multiplier system
- **URINARY BLADDER**
- **URETHRA**
  - **Male urethra**
    - Preprostatic
    - Prostatic
    - Membranous
    - Spongiose part
  - **Female urethra**

- Physiology
  - Micturition
  - Concentration /dilution of urine
    - Medullary gradient
    - Role of ADH
  - Composition of urine
  - Kidney function tests
    - Urine examination
    - Blood urea estimation
    - Serum creatinine estimation
    - Other blood tests
    - GFR
    - Plasma clearance
    - Measurement of renal blood flow
    - Measurement of RPF

KIDNEY DISEASES

- Glomerulonephritis
- Pyelonephritis
- Acute renal failure
- Chronic renal failure
- Nephrotic syndrome
- Uremia
- Calculi
- Diabetic kidney
- Renal hypertension
- Tumors

ARTIFICIAL KIDNEY

PRINCIPLE

- Dialysis
  - Indications for dialysis
    - In ARF
      - Biochemical indications
      - Clinical indications
    - In CRF
      - Biochemical indications
      - Clinical indications
  - Types of dialysis
    - Hemodialysis
      - Complications
        - Acute
        - Chronic
    - CAPD
      - Advantages
      - Complications

- Renal Transplant
  - Patient selection and
    - Laboratory studies
    - Radiological studies
    - Donor
      - Evaluation of donor
      - Contraindications to donation
  - Post-operative care
  - Immunosuppression
  - Contraindications
    - Absolute
    - Relative
  - Rejection
  - Complications

Introduction

Excretion means removal of waste products from the body. Kidneys, sweat glands, lungs, rectum and liver are the chief organs of excretion. The primary organs are the kidneys. Carbon dioxide and water vapor are removed by the lungs. Kidneys and sweat glands (skin) excrete urea, uric acid, various salts and other nitrogenous waste.

The main organs of the urinary system are

- 2 kidneys
- 2 ureters
- 1 urinary bladder
- 1 urethra

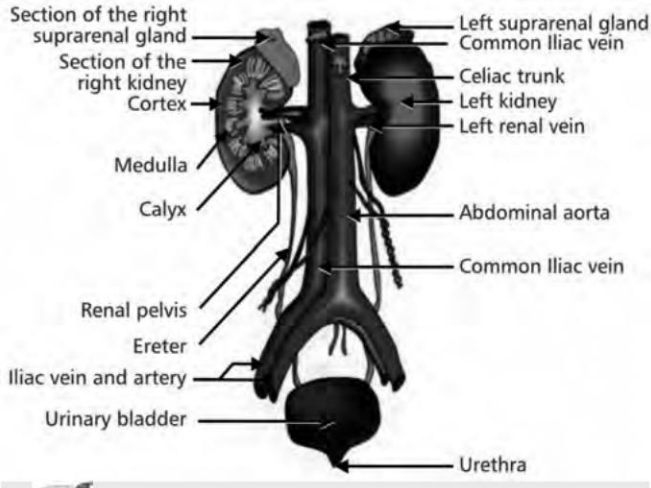


Fig. 13.1 *Urinary system (Refer colour figure)*

13.1 KIDNEYS

The kidneys are complex organs having numerous biological roles. Their primary role is to maintain the homeostatic balance of bodily fluids by filtering and secreting metabolites (such as urea) and minerals from the blood and excreting them, along with water, as urine. It, thus, maintains the internal environment.

13.1.1 Anatomy

1. Organs Related to the Kidneys

The kidneys lie on either side of the vertebral column. Each is related to different structures.The right kidney is covered superiorly by the right adrenal gland; posteriorly it is related to the diaphragm and the muscles of the posterior abdominal wall. Anteriorly are the hepatic flexure of colon, duodenum and the right lobe of the liver.

The left kidney has the left adrenal gland superiorly. Posteriorly are the diaphragm and the muscles of the posterior abdominal wall. Anteriorly are the spleen, stomach, pancreas, splenic flexure of colon and the jejunum.

2. Structure of the Kidney

The kidneys are located in the posterior part of the abdominal cavity. There are two, one on each side of the spine, behind the peritoneum and below the diaphragm. They extend from the level of the 12th thoracic vertebra to the 3rd lumbar vertebra. The asymmetry within the abdominal cavity is caused by the liver which results in the right kidney being slightly lower than the left one. The left kidney is located slightly more medial than the right one.

Kidneys are bean-shaped organs. They are dark reddish-brown in color due to the presence of many blood vessels. Each kidney is about 11 cm long, 6 cm wide and 3 cm thick and weighs around 150 g. The upper part of the kidneys is partially protected by the eleventh and twelfth ribs. Each kidney with the adrenal gland are surrounded by two layers of fat (the perirenal and pararenal fat) and the renal fascia which help to cushion it.

3. Macroscopic Structure of the Kidney

The kidney is a compound tubular gland. The hilum forms the major part of the medial border which is concave and depressed. Renal artery, renal veins, nerves and the ureter pass through this hilum.

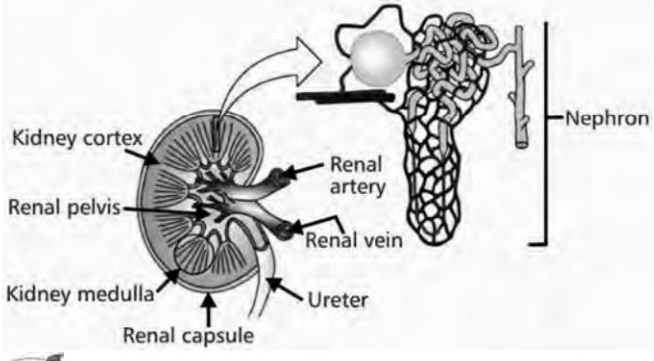


Fig. 13.2 *Structure of a kidney (Refer colour figure)*

The kidney is divided into three areas of tissue—an outer cortex, a middle medulla and an inner pelvis. 20% of blood pumped by the heart passes through the kidneys. A fibrous capsule surrounds the kidney.

(a) Cortex The cortex lies just below the capsule of the kidney and is reddish brown in color and granular in appearance.

The cortex contains convoluted tubules and corpuscles. At places, the cortical tissue goes into the medulla and forms columns which are called **columns of Bertini**.

(b) Medulla The medulla is the inner layer. It contains conical striations, which gives the medulla a radially striated appearance. These are called **pyramids**, which vary from 8 to 20 in number. The medulla has vascular and tubular structures which are arranged parallel to one another. The apex of the pyramid is towards the minor calyx and the broad base of the pyramid is towards the cortex.

(c) Renal Sinus (Renal Pelvis) The renal sinus is funnel-shaped and is the upper expanded part of the ureter. It is also called the **renal pelvis**. It has major and minor branches, called **calyces**. There are 3 to 4 major calyces and 8 minor calyces, and these calyces surround the apex of the pyramids. The pelvis also contains branches of nerves and arteries and veins with loose connective tissue and fat in between.

The walls of the pelvis are made of smooth muscle and lined by a transitional epithelium. Urine, which is formed in the kidney, passes from the pelvis into the ureter due to peristaltic movements of these smooth muscles.

(d) Arterial Supply Right and left renal arteries, which divide into segmental arteries; they then form interlobal arteries and arcuate arteries; they divide further to form interlobular arteries and they give off branches in the renal cortex called afferent arterioles.

(e) Venous Drainage Efferent arteriole is formed from the glomerular capillaries. Efferent arterioles unite to form peritubular capillaries which further unite to form peritubular venules and then interlobular veins. The arcuate veins are now formed which drain blood into interlobar veins which finally forms the renal vein. It leaves the renal hilum and empties into the inferior vena cava.

(f) Lymphatic Drainage From the right kidney, lymphatics go on the anterior aspect of the inferior vena cava and to the nodes near the aortic bifurcation and empty into the thoracic duct. From the left kidney, lymphatics go to the lateral aortic nodes and the celiac and iliac nodes and empty into the thoracic duct.

(g) Nerve Supply Renal nerves arise from the celiac ganglion and pass through the renal plexus into the kidneys. They are sympathetic nerves. They regulate the blood flow through the kidney by causing vasodilatation or vasoconstriction of renal arteries.

4. Microscopic Structure of the Kidney

The parenchyma of the kidney consists of nearly one million functional units called the **nephrons**. There are also a smaller number of collecting tubules which carry urine from the nephrons through the pyramid and pour it into the pelvis. These collecting tubules give a striated appearance. The blood vessels, interstitial connective tissue, nerves and lymph vessels are seen in between the tubules.

The collecting ducts unite to form ducts of Belini which open into minor calyces.

(a) Nephron A nephron is the structural and functional unit of the kidney, responsible for the actual filtration (and thereby purification) of the blood. There are about one million nephrons in the cortex of each kidney, and each one consists of a renal corpuscle and a renal tubule which carry out the functions of the nephron. The nephron is part of the homeostatic mechanism which helps in regulating the amount of water, salts, glucose, urea and other minerals in the body. The nephron is the basic unit responsible for filtration as well as reabsorption of water and salts. Each nephron consists of a tubule closed at one end. The other end opens into a collecting tubule. The blind end is indented to form a cup-shaped Bowman's capsule which encloses the glomerulus, which is a network of capillaries.

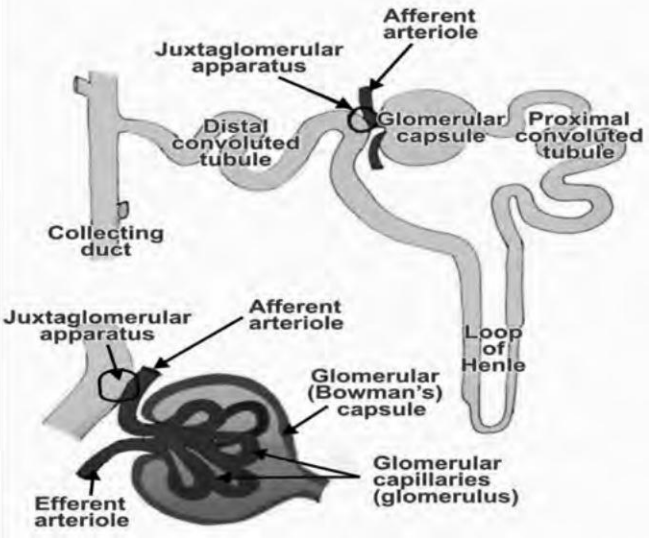


Fig. 13.3 *Nephron*

Each nephron has a length of about 3 cm. It is differentiated into 4 regions having different anatomical features and different physiological roles. The 4 regions are

1. Bowman's capsule
2. Proximal convoluted tubule
3. Loop of Henle
4. Distal convoluted tubule

(i) Bowman's Capsule It is a large double-layered cup which lies in the renal cortex. It encloses a tuft of capillaries called **glomerulus**.The outer layer is continuous with the rest of the nephron. The space between the two layers of the Bowman's capsule is continuous with the lumen of the next part of the nephron. The Bowman's capsule and the glomerulus together are called the **renal corpuscle** or **Malphigian body**.

(ii) Proximal Convoluted Tubule It starts from the neck of the Bowman's capsule, it is highly convoluted and occupies the renal cortex. Its length is 14 mm and diameter is 55 u. The

wall consists of a single layer of columnar cells. These cells bear hairlike projections called **microvilli**. They are, hence, called **brush cells**.

(iii) Loop of Henle It is a V-shaped segment of the nephron located in the renal medulla. It consists of two straight parallel limbs: a descending limb which is a direct continuation of the proximal convoluted tubule and an ascending limb. The ascending limb enters the renal medulla and the descending limb re-enters the renal cortex and joins the distal convoluted tubule.

(iv) Distal Convoluted Tubules The distal convoluted tubule is greatly coiled. The terminal part opens into the collecting duct and is called the collecting tubule. The collecting ducts receive the collecting tubules of many other nephrons. They join and form the large ducts of Belini which open into the papilla of minor calyces. Three to four minor calyces join to form one major calyx. Major calyces open into the renal pelvis.

(b) Histology The bowman's capsule consists of a single layer of flattened epithelial cells on a basement membrane. The proximal convoluted tubule is lined by a single layer of cuboidal epithelial cells with hairlike projections. The thick descending segment is formed by brush-bordered cuboidal epithelial cells. The thick ascending segment and the distal convoluted tubule are both lined by cuboidal epithelial cells without brush border. The collecting duct is lined by cuboidal or columnar epithelial cells.

(c) Glomerulus The glomerulus is the main filter of the nephron and is located within the Bowman's capsule. It resembles a twisted-coiled mass of tiny tubes through which the blood passes. It is semipermeable, allowing water and soluble wastes to pass through and be excreted out of the Bowman's capsule as urine. The filtered blood passes out of the glomerulus into the efferent arteriole, to be returned through the medullary plexus to the intralobular vein.

The renal artery at the hilum divides into smaller arteries which again divide into arterioles. The capillaries arise from the afferent arteriole. Each large capillary divides and subdivides into small capillaries which are arranged as irregular loops. They, then, form a cluster of capillaries. Between the loops there are connective tissue-phagocytic mesangial cells. The capillaries unite to form the efferent arteriole. This again breaks up into a second capillary network which supplies oxygen and nutrients to the remaining part of the nephron. Venous blood draining from this capillary bed opens into the renal vein which finally drains into the inferior vena cava.

The diameter of the afferent arteriole is bigger than the diameter of the efferent arteriole. Capillaries consist of a single layer of endothelial cells with pores in between, which are called slit pores.

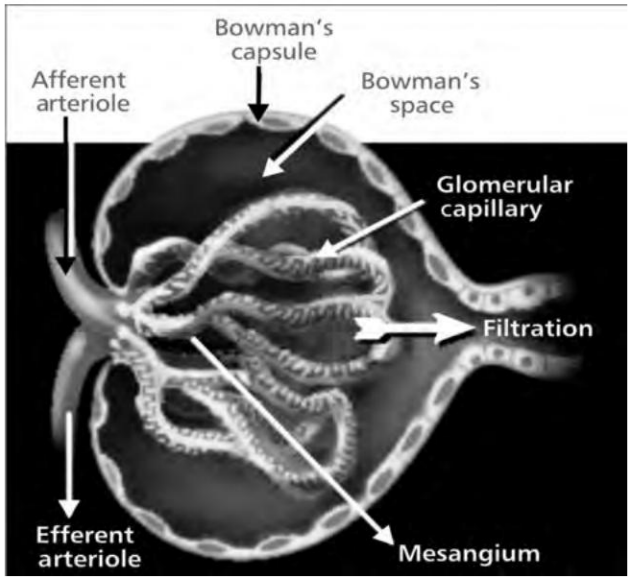


Fig. 13.4 *Bowman's capsule*

The glomerular walls are more permeable than those of other capillaries.

(d) Juxtaglomerular Apparatus The juxtaglomerular apparatus is a microscopic structure in the kidney. It regulates the function of each nephron. It is found between the vascular pole of the renal corpuscle and the returning distal convoluted tubule of the same nephron, i.e., near the glomerulus; hence it is called the juxtaglomerular apparatus.

The juxtaglomerular apparatus secretes renin and erythropoietin. The role of renin has been discussed in detail elsewhere. Erythropoietin helps in erythropoiesis by stimulating the bone marrow.

The main function of this apparatus is to carry out its function of regulating renal blood flow and glomerular filtration rate.

The apparatus is made up of three cellular components. They are the macula densa, extraglomerular mesangial cells, and juxtaglomerular cells (also known as granular cells).

5. Functions of the Kidney

The kidney performs a wide range of vital functions in the body, viz., regulating fluid and electrolyte balance by filtration, secretion and reabsorption. It removes waste and excess water from the blood. Thus, it balances levels of various important biochemical substances, minerals and electrolytes in the body.

The kidney also acts like an endocrine organ—it activates both erythropoietin (for production of red blood cells) and vitamin D (which regulates calcium metabolism) and keeps the bones strong and healthy. It also produces renin (in the afferent arteriole) which affects various aspects of water and electrolyte homeostasis. It, thus, helps in controlling blood pressure.

13.1.2 Physiology

1. Physiology of Formation of Urine

Kidneys are the organs which form urine. The production of urine is vital to the health of the body. Urine is composed of water, certain electrolytes, and various waste products that are filtered out of the blood system. Urine formed in the kidney passes through the ureter into the urinary bladder and is stored there. From here, it is disposed of via the urethra.

Metabolism in the tissues results in the formation of waste, which is removed by blood from tissue. A major part of the cleaning of the blood takes place in the kidney.

Urine formation includes three processes:

(a) Glomerular filtration
(b) Selective reabsorption
(c) Tubular secretion

(a) Glomerular Filtration As blood passes through the glomeruli, much of its fluid, containing both useful biochemical substances and dissolved waste materials, come out of the blood through the membranes (by osmosis and diffusion) where it is filtered and then flows into the Bowman's capsule. This process is called glomerular filtration.

The filtered fluid is called glomerular filtrate. Water and small molecular substances pass through, but blood cells and plasma proteins are not filtered. The filtrate in the glomerulus has a composition nearly similar to plasma minus blood cells and plasma proteins.

The substances during filtration pass through the endothelium of glomerular capillary membrane, basement membrane and the space between the cells of the visceral layer of Bowman's capsule.

This filtration is helped by the pressure difference of blood in the glomerulus and pressure of filtrate in the glomerular capsule. The pressures determining glomerular filtration are the glomerular capillary pressure, colloidal osmotic pressure in the glomeruli and hydrostatic pressure in the Bowman's capsule.

Renal blood flow is maintained by auto-regulation mechanism, which has a direct effect on filtration. Renal blood flow is maintained at a constant pressure and works independent of nervous control. It may be stimulated by changes in the blood pressure in the renal arteries. Auto-regulation fails when systolic blood pressure falls below 80 mmHg, e.g., in shock. The renal blood flow and hydrostatic pressure decrease and filtration is impaired.

The total Glomerular Filtration Rate (GFR) for the whole body (i.e., for all of the nephrons in both kidneys) is normally about 125 mL per minute. Urine formed per day (24 hours) is 1 to 1.5 liters.

GFR can be affected by blood pressure, renal blood flow, sympathetic stimulation and constriction of afferent or efferent arteriole.

(b) Selective Reabsorption Reabsorption, by definition, is the movement of filtered substances out of the renal tubules, back into the peritubular blood capillaries, located around the tubules. Substances reabsorbed are water, glucose, salts and other miscellaneous substances. Reabsorption begins in the proximal convoluted tubules and continues in the loop of Henle, distal convoluted tubules, and collecting tubules. This is necessary to maintain fluid and electrolyte balance and to maintain the pH of blood, i.e., to maintain homeostasis.

Reabsorption is of two types:

- Active transport
- Passive reabsorption

Active transport is carried out at carrier sites in the epithelial membrane. There is movement of molecules against the electrochemical gradient. Chemical energy is used to transport the substances against their concentration gradients. Energy is derived from ATP.

The substances which are actively reabsorbed are sodium, calcium, potassium, glucose, amino acids, bicarbonates, sulfates, phosphates, uric acid, ascorbic acid and ketone bodies. Nutrients like glucose (blood sugar) are entirely reabsorbed back into the blood from the proximal tubules. It is actively transported out of the tubules and into the peritubular capillary blood.

Large amounts of water—more than 178 liters per day—are reabsorbed into the bloodstream from the proximal tubules because the physical forces acting on the water in these tubules actually push most of the water back into the blood capillaries. About 99% of the 180 liters of water that leave the blood each day by glomerular filtration, return to the blood from the proximal tubule through the process of **passive reabsorption**. Other substances reabsorbed by passive transport are chloride and urea.

Some ions like sodium and chloride can be absorbed by both active and passive mechanisms depending from where they get absorbed, i.e., site of the nephron.

This reabsorption of substances depends on the needs of the body and in some cases is regulated by hormones, e.g., calcium and phosphate reabsorption are regulated by parathyroid hormone and calcitonin. Water reabsorption is increased by the antidiuretic hormone which increases permeability of the distal convoluted tubules and collecting tubules. Aldosterone increases reabsorption of sodium and excretion of potassium.

Urea and uric acid are reabsorbed minimally, and the substances which are not normal constituents of blood are not reabsorbed at all.

(c) Tubular Secretion Secretion is the process by which substances move into the distal and collecting tubules from

blood in the capillaries around these tubules. Secretion is the reverse of reabsorption. Whereas reabsorption moves substances out of the tubules and into the blood, secretion moves substances out of the blood into the tubules, where they mix with the water and other wastes and are passed in the urine. These substances are secreted through either an active transport mechanism or as a result of diffusion across the membrane.

If blood flows quickly through the glomerulus then, certain substances which are not required, e.g., aspirin, may not be cleared by filtration. This is because the blood remains for a very short period in the glomerulus. So these substances are secreted into the lumen of the convoluted tubules and thereby it enhances excretion. Secretion of hydrogen is important for the maintenance of homeostasis. Hydrogen is secreted in the proximal and distal convoluted tubules. Other substances secreted are potassium and ammonia.

Thus, urine is formed by the processes of filtration, reabsorption and secretion. Urine from the renal calyx comes into the ureter and finally into the urinary bladder, where it is stored. When a bladder becomes full, the sensation of micturition develops and urine is voided out.

2. Counter-current Multiplier System

The descending limb of the loop of Henle carries tubular fluid from the renal cortex into the medulla and the ascending limb carries it in the opposite direction. Hence, fluid flowing in one tube is in an opposite direction to the fluid flowing in the parallel tube and thus, flow of fluid is in the opposite direction in the two limbs of the loop of Henle.

The loop of Henle and the vasa recta form the counter current system. Hence, it is called the counter-current system.

The ascending limb of the loop of Henle is impermeable to water but transport solutes Na^+ and Cl^- out of the tubule lumen. Active transport of Cl^- takes place which is followed passively by Na^+. So osmolarity of tubular fluid decreases as it flows through the ascending limb. This is called **single effect**. The osmolarity of the interstitium rises progressively from cortex to medulla through multiplication of this single effect by concurrent flow. The osmolarity of tubular fluid falls at the junction of the medulla and cortex even up to 100 mOsm/liter.

The descending limb is permeable to water. Water moves out of the descending limb by osmosis. So the osmolarity of tubular fluid increases and as it goes along the descending limb, the osmolarity increases further till at the hairpin bend, the osmolarity is 1200 mOsm/liter.

The overall effect is that the tubular fluid becomes more concentrated when it passes through the descending limb and more dilute as it passes through the ascending limb.

Counter-current exchange of solutes between ascending and descending vasa recta (the renal medullary capillaries) minimizes solute wash-out from the medullary interstitium.

The mechanism of counter-current multiplication works together with the vasa recta's counter-current exchange to prevent the wash-out of salts and maintain a high osmolarity at the inner medulla.

13.2 URINARY BLADDER

The urinary bladder is a baglike, muscular and distensible (elastic) organ that lies on the pelvic floor. It is the organ that collects urine excreted by the kidneys prior to its disposal by urination. Urine enters the bladder via the ureters and exits via the urethra.

In males, the base of the bladder lies between the rectum and the pubic symphysis. It is superior to the prostate, and separated from the rectum by the rectovesical recess.

In females, the bladder is inferior to the uterus and anterior to the vagina. It is separated from the uterus by the vesicouterine recess.

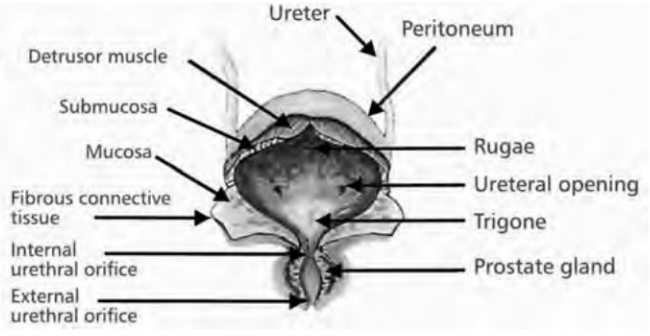


Fig. 13.5 *Urinary bladder and urethra*

The fundus of the urinary bladder is the base of the bladder, formed by the posterior wall. The peritoneum lies superior to the fundus.

The detrusor muscle is a layer of the urinary-bladder wall made of smooth muscle fibers arranged in spiral, longitudinal, and circular bundles. When the bladder is stretched, impulses are sent to the parasympathetic nervous system, resulting in the contraction of the detrusor muscle. This encourages the bladder to expel urine through the urethra.

For the urine to exit from the bladder, both the autonomically controlled internal sphincter and the voluntarily controlled external sphincter must be opened. Problems with these muscles can lead to incontinence. If the amount of urine reaches 100% of the urinary-bladder volume, the voluntary sphincter becomes involuntary and the urine will be ejected instantly, although it is possible to hold it for some time in order to prevent urination.

The urinary bladder usually holds 400–620 mL of urine, but it can hold twice this amount without rupturing it, e.g., in the outflow tract obstruction.

The desire to urinate usually starts when the bladder reaches around 25% of its capacity.

The urinary bladder has a transitional epithelium that is continuous with that in the ureters. It does not produce mucus. When the bladder is empty, the mucosa has numerous folds called rugae. The **rugae** and transitional epithelium allow the bladder to expand as it gets filled up.

The second layer in the walls is the **submucosa** that supports the mucous membrane. It is composed of connective tissue with elastic fibers.

The next layer is the **muscularis**, which is composed of smooth muscle. The smooth muscle fibers are interwoven in all directions and collectively these are called the **detrusor muscle**. Contraction of this muscle expels urine from the bladder. On the superior surface, the outer layer of the bladder wall is parietal peritoneum. In all other regions, the outer layer is fibrous connective tissue.

There is a triangular area, called the **trigone**, formed by three openings in the floor of the urinary bladder. Two of the openings are from the ureters from each side and form the base of the trigone. Small flaps of mucosa cover these openings and act as valves that allow urine to enter the bladder but prevent backflow of urine from the bladder into the ureters. The third opening, at the apex of the trigone, is the opening into the urethra. A band of the detrusor muscle encircles this opening to form the **internal urethral sphincter**.

(a) Arterial Supply The main arteries supplying the bladder are branches of the internal iliac arteries. The superior vesicle artery, branches of the umbilical artery supply the anterosuperior parts of the bladder. The inferior vesicle arteries (in males) or vaginal arteries (in females), as also branches of the internal iliac arteries, supply the base of the bladder. The obturator and inferior gluteal arteries also supply small branches to the bladder.

(b) Venous Drainage The veins form a venous plexus on the inferolateral surface and drain the blood to the internal iliac vein.

(c) Lymphatic Drainage The lymph vessels from the superior part of the bladder pass to the external iliac lymph nodes. Those from the inferior part of the bladder pass to the internal iliac lymph nodes. Some lymph vessels from the neck region of the bladder drain into the sacral or common iliac lymph nodes.

(d) Nerve Supply

- **The efferent fibers**
  1. Parasympathetic supply is from the S_{2-4} segments of the spinal cord. These enter the inferior hypogastric plexus and pass through it to the bladder wall.

     They are motor to the detrusor and inhibitory to the internal sphincter.
  2. Sympathetic supply is from the T_{11-12}, L_{1-2} segments of the spinal cord.

     These synapse in the inferior hypogastric plexus and the postganglionic fibers pass to the bladder. They cause constriction in the internal sphincter and inhibit the detrusor muscle.
- **The afferent fibers**

  These are concerned with the awareness of distension and pain.

  They pass back to the CNS via both the sympathetic and parasympathetic nerves.

13.3 URETHRA

The urethra is the tube through which urine leaves the body. It begins at the neck of the bladder, traverses the pelvic and urogenital diaphragms, and ends at the external urethral orifice where it opens. In men, the urethra is within the penis.

13.3.1 Male Urethra

In the male, the urethra is about 18–20 cm long and it extends from the internal urethral orifice in the bladder to the external meatus on the tip of the penis.

It may be divided into 4 parts: the preprostatic, prostatic, membranous and spongiose.

(a) The Preprostatic Part This part possesses a stellate lumen and is only 1.5 cm long. It extends from the internal urethral orifice to the superior aspect of the prostate.

Smooth muscle surrounding the bladder neck and preprostatic urethra is circular and is known as the internal sphincter. This is richly supplied with sympathetic noradrenergic fibers.

(b) The Prostatic Part This is 3–4 cm long and has a midline ridge on its posterior wall known as the **urethral crest**. On each side of the crest is a groove known as the **prostatic sinus**, into which the orifices of the prostatic ducts open.

There is an elevation on the urethral crest about halfway down which is known as the **collicus seminalis**. On the summit of this, the prostatic utricle opens which is 6 mm long and is the remnant of the paramesonephric ducts. On either side of the utricle are the openings of the ejaculatory ducts.

(c) The Membranous Part This is the shortest part (2 cm) and the least dilatable part and passes through the urogenital diaphragm. The external sphincter, or sphincter urethrae, is derived from the urogenital diaphragm musculature. The sphincter urethrae is supplied by the perineal branches of the pudendal nerve (S_{2-4}).

(d) The Spongiose Part This part is contained within the corpus spongiosum of the penis. It is dilated at its beginning as

the intrabulbar fossa, and again within the glans of the penis as the navicular fossa. The ducts of the bulb urethral gland open into the spongiose part below the perineal membrane.

The external urethral orifice is the narrowest part of the urethra.

There are several recesses in the urethra known as lacunae. Mucous glands, known as urethral glands, open into this part of the urethra.

The superficial vascular supply to the penis comes from the external pudendal vessels, which arise from the femoral vessels. The deep penile structures receive their arterial supply from the common penile artery, which arises from the internal pudendal artery.

13.3.2 Female Urethra

1. The female urethra is only 4 cm long and opens at the external urethral orifice.
2. This is about 2.5 cm behind the glans clitoris and directly in front of the vaginal opening.
3. The female urethra has a posterior longitudinal fold and external and internal sphincters.

The blood supply is from the superior and inferior vesical branches of the internal iliac artery.

13.3.3 Physiology

1. Micturition

Micturition is also known as urination. It is the process of disposing urine from the urinary bladder through the urethra to the outside of the body. The process of urination is under voluntary control; in infants and individuals with neurological injury, urination may occur as an involuntary reflex.

The main organs involved in urination are the bladder and the urethra. The urinary bladder acts as a reservoir of urine. The smooth muscle of the bladder, known as the detrusor, has both sympathetic and parasympathetic innervation. Sympathetic innervation is from $T_{11\text{-}12}$, $L_{1\text{-}2}$ segments of the spinal cord. Parasympathetic supply is from 2nd, 3rd and 4th sacral segments. Stimulation of sympathetic nerve causes relaxation of the detrusor muscle while stimulation of parasympathetic fibers causes relaxation of the internal sphincter. The external urinary sphincter is innervated by somatic fibers from 2nd, 3rd and 4th sacral segments.

In infants, voiding occurs involuntarily (as a reflex). The ability to voluntarily inhibit micturition develops at the age of 2–3 years. There are two discrete phases of activity: the storage phase, when urine is stored in the bladder; and the voiding phase, when urine is released through the urethra. The state of the reflex system is dependent on both a conscious signal from the brain and the firing rate of sensory fibers from the bladder and urethra.

The urinary bladder acts as a reservoir of urine. Micturition reflex starts when 300 to 400 mL of urine accumulates in the urinary bladder.

The wall of the bladder has stretch receptors. They are stimulated and sensory impulses reach the sacral segments of the spinal cord. Autonomic efferent (motor) impulses are conveyed to the bladder and the internal sphincter. There is contraction of the detrusor muscle and relaxation of the internal urethral sphincter. There are also stretch receptors in the urethra. When urine enters the urethra, these receptors are stimulated, afferent impulses are sent to spinal cord, efferent impulses are conveyed and the external sphincter relaxes and there is voiding of urine. This is also helped by increasing the pressure in the pelvic cavity. This is achieved by contracting the abdominal muscles.

2. Concentration and Dilution of Urine

The ability of the kidney to form urine, which is more concentrated than plasma, is necessary for survival.

Osmolarity of glomerular filtrate is 300 milliosmoles/liter, which is equal to that of plasma. The osmolarity of urine is 4 times of this, i.e., 1200 milliosmoles/liter.

Water is continuously lost from the body through various routes, e.g., lungs, skin, gastrointestinal tract and kidneys. When there is a water deficit in the body, the kidneys form concentrated urine by continuing to excrete solutes while increasing water reabsorption and decreasing the volume of urine.

This formation of concentrated or dilute urine depends upon

(a) Medullary gradient
(b) Antidiuretic Hormone (ADH) mechanism

(a) Medullary Gradient The osmolarity of interstitial fluid, in almost all parts of the body, is about 300 milliosmoles/liter, while the osmolarity of the interstitial fluid in the medulla of the kidney is 1200 milliosmoles/liter; so from the cortex till it reaches the inner part of medulla, the osmolarity goes up from 300 to 1200 milliosmoles/liter. This gradual increase in the osmolarity of the medullary interstitial fluid is known as medullary gradient.

The various factors which are responsible for the formation of concentrated urine are the following:

1. Active reabsorption of sodium and co-transport of potassium, chloride and other ions, when the filtrate passes through the proximal convoluted tubule; there is obligatory reabsorption of water
2. Active transport of ions from the collecting ducts into medullary interstitium
3. Passive diffusion of large amounts of urea from the inner medullary collecting ducts into the medullary interstitium

4. Diffusion of only small amounts of water from the medullary tubules into the medullary interstitium

Of all these factors, the most important cause of the high medullary osmolarity is active transport of sodium and co-transport of potassium, chloride and other ions.

When fluid passes from the proximal convoluted tubule into the thick descending segments, water is reabsorbed into medullary interstitium. Here, the osmolarity goes up to 600 milliosmoles/liter.

The thin descending segment is very permeable to water and hence when the fluid comes here, more water is reabsorbed. So, tubular fluid osmolarity becomes equal to renal medullary osmolarity.

The thin ascending segment is impermeable to water, but reabsorbs some sodium chloride; so tubular fluid becomes more dilute as water remains in the tubule and sodium chloride diffuses out.

Some of the urea absorbed into the medullary interstitium from the collecting ducts, also diffuses into the ascending limb; so, urea is returned to the tubular system. The recycling of urea also helps to the medullar hyperosmolarity.

The thick ascending segment is also impermeable to water. But here, there is active reabsorption of sodium and chloride. Therefore, fluid in the thick ascending limb of loop of Henle becomes very dilute.

The distal convoluted tubule and collecting duct are totally impermeable to water but permeable to solutes. As a result, sodium and chloride are reabsorbed. In presence of ADH, these segments become permeable to water; so from the distal convoluted tubule and collecting duct, water reabsorption is induced by this hormone. This is known as facultative reabsorption of water.

A large quantity of water is removed from the fluid while passing through these segments. The urine, here, becomes hypertonic with an osmolarity of 1200 milliosmoles/liter.

Thus, a very concentrated but small volume of urine is produced when ADH levels are high. Water reabsorption increases urea concentration in the tubular fluid. The inner medullary collecting ducts are highly permeable to urea. So urea diffuses out of the tubular lumen into the medullary interstitium. This absorption of urea into the renal medulla also contributes to the high osmolarity of the medullary interstitium.

(b) Mechanism of Action of Antidiuretic Hormone (ADH) The main effect of the antidiuretic hormone is to reduce urine output. It increases the permeability to water of the distal convoluted and collecting tubules of the nephrons. The facultative reabsorption of water from the glomerular filtrate is increased.

ADH secretion depends on the osmotic pressure of blood around the osmoreceptors in the hypothalamus. When this pressure is more, ADH secretion increases and more water is reabsorbed; thus urine output decreases. The pressure comes down. In the same way, when osmotic pressure decreases, ADH secretion decreases, water reabsorption decreases and urine output increases.

3. Composition of Urine

Urine is the end product of metabolism of billions of human cells.

Urinary volume is dependent upon fluid intake; the amount of solutes to be excreted, primarily sodium and urea; loss of body fluids by normal processes, such as perspiration and respiration, cardiovascular and renal function.

Fresh urine has an inoffensive odor. Normal urine has a pale yellow color and is clear.

Its normal specific gravity is 1.005 to 1.025, and the normal pH of urine is 4.3 to 8.0.

Urine contains the following:

- 96% is water.
- Urea is 2%.
- Rest of the 2% is sodium, potassium, chlorides, sulphates, phosphates, ammonia, uric acid and creatinine.

In urine, there are either no proteins or just traces of proteins.

Healthy individuals normally will have no detectable sugars, ketones, blood, myoglobin or bilirubin in their urine.

Microscopic Examination In healthy people, the urine contains small numbers of cells and other formed elements and epithelial cells.

There is an occasional red blood cell in the urine (2–3 per high power field).

Urine stored in the bladder is normally free of bacteria or yeast.

A few hyaline casts are normal, and epithelial cells are a common ingredient of urine sediment.

Healthy people often have only a few crystals in their urine.

4. Kidney Function Tests

The diagnosis of a majority of renal disorders can be made by the history of the patient, clinical examination and urine examination. Renal function tests are carried out

- to detect renal insufficiency
- to estimate the degree of kidney damage
- to know whether the changes are permanent

(a) Urine Examination Urine examination is one of the oldest and most preliminary procedures carried out in medicine.

Physical Examination Urine is seen for odor, color and clarity. Volume, osmolality and specific gravity are measured.

Chemical Examination Urinary pH is measured.

Routine examination is done for presence of proteins, sugar, ketones, blood, myoglobin, bilirubin and nitrites.

Microscopic Examination Urine sediment is assessed for red blood cells, white blood cells, bacteria, casts, yeast, crystals and epithelial cells.

(b) Blood Urea Estimation Blood urea is the principal end product of the protein catabolism. The normal value is 25 to 40 mgm %. Elevation of blood urea is evidence of impairment of renal function, but does not necessarily mean structural disease of the kidney. It is affected by extra renal factors also, e.g., low B.P., dehydration, etc.

(c) Serum Creatinine Estimation Measuring serum creatinine is a useful and inexpensive method of evaluating renal dysfunction. Creatinine is freely filtered and, therefore, the serum creatinine level depends on the Glomerular Filtration Rate (GFR). Renal dysfunction diminishes the ability to filter creatinine, so the serum creatinine rises. If the serum creatinine level doubles, the GFR is considered to have been halved. The normal value is 0.5 to 1.5 mgm %. In renal failure, the value is raised. This test reflects the structural integrity of the kidney; therefore it is more reliable than blood urea estimation.

(d) Other Blood Tests Measurement of the blood levels of other elements, regulated in part by the kidneys, can also be useful in evaluating kidney function. These include serum sodium, potassium, chloride, bicarbonate, calcium, magnesium, phosphorus, protein, uric acid, and blood glucose.

(e) Glomerular Filtration Rate (GFR) GFR is a test of how much the kidneys are filtering. It is normally about 100 mL/minute. This means that the kidneys are removing all the creatinine found in 100 mL of blood every minute—almost 150 liters per day. Most of this is absorbed back into the body, so that only 1–2% of the filtrate appears as urine. Creatinine clearance gives quite a good measure of GFR, but requires a 24-hour urine collection for measurement.

Creatinine clearance is used to measure GFR, as it is already present in body fluids and its plasma concentration is steady throughout the day.

GFR is calculated from the formula

$$GFR = UV/P$$

where

U = Concentration of creatinine in urine
= 125 mgm%
V = Plasma concentration of creatinine = 1 mgm
P = Volume of urine excreted = 1 mL/min
$125 \times 1/1 = 125$ mL/min

(f) Plasma Clearance The volume of plasma completely cleared of a specific compound per unit time is measured as a test of kidney function.

If we can determine the clearance value of certain substances then some of the renal functions can be assessed.

Formula to calculate clearance value is

$$C = UV/P$$

where

C = Clearance
U = Concentration of the substance in urine
V = Volume of urine flow
P = Concentration of the substance in blood

(g) Measurement of Renal Blood Flow No ideal technique exists for measurement of renal blood flow in man. An accepted method applies the **Fick Principle** to determine blood flow through clearance. Total renal blood flow can be measured by estimating the clearance of a substance that is completely removed from the blood in a single pass through the kidney.

Such a substance is Para-Aminohippurate (PAH), which is cleared from the blood by a combination of filtration and, tubular secretion. PAH is not reabsorbed, metabolized or synthesized by the kidney.

Renal blood volume is calculated from the formula

$$RBF = \frac{\text{Renal plasma flow} \times 100}{100 - \text{PCV}}$$

Here, PCV is 45%.

Supposing renal plasma flow is 660 mL/min

$$\text{Then } \frac{660 \times 100}{55}$$

$$= 1200 \text{ mL/min}$$

So, renal blood flow is 1200 mL/min

(h) Measurement of Renal Plasma Flow (RPF) Renal plasma flow is the volume of blood plasma delivered to the kidneys per unit time.

A substance which is filtered and secreted but not reabsorbed should be used to measure renal plasma flow. PAH (Para-Amino Hippurate) clearance is used to calculate the effective Renal Plasma Flow (eRPF). PAH is freely filtered, and it is not reabsorbed by the kidney so that its venous plasma concentration is approximately zero.

A known amount of PAH is injected into the body. Concentration of PAH in plasma and urine are estimated and the volume of urine excreted is calculated.

The equation for renal clearance for PAH is

$$eRPF = \frac{U_{PAH}}{P_{PAH}} V$$

where, the concentration of PAH in urine is 66 mgm %;
Plasma concentration is 0.1 mgm %.
Volume of urine excreted is 1 mL/min

Then

$$\text{Renal plasma flow} = \frac{66 \times 1}{0.1}$$

$$= 660 \text{ mL/min}$$

So, renal plasma flow is 660 ml/min

(i) Other Tests If blood and urine tests indicate reduced kidney function, additional tests can be done to help identify the cause of the problem. These are the following:

(i) Renal Imaging Methods of renal imaging (taking pictures of the kidneys) include ultrasound, computed tomography (CT scan), and Magnetic Resonance Imaging (MRI). These tools are most helpful in finding new growths in the kidney or blockages to the flow of urine.

(ii) Renal Biopsy Renal biopsy is a hospital procedure in which the doctor inserts a needle through the skin to approach the posterior side of the kidney. The needle retrieves a strand of tissue about 1/2 to 3/4 of an inch. The patient will lie on his stomach on a table and receive local anesthetic to numb the skin. The sample tissue will help the doctor identify problems at the cellular (histological) level.

13.4 KIDNEY DISEASES

1. Glomerulonephritis

Glomerulonephritis is a renal disease characterized by inflammation of the glomeruli. It could be focal or diffuse, acute or chronic, proliferative or membranous.

Pathophysiology The exact reason is not clearly understood. Etiologies may vary; however, majority of the cases are idiopathic. It can follow streptococcal infection—usually upper respiratory tract infection. A link between hemolytic streptococci and acute glomerulonephritis has been recognized in the 20th century. Probably, immunological mechanisms trigger inflammation of the glomerulus and also the proliferation of glomerular tissue resulting into basement membrane mesangium and capillary endothelium damage.

Many patients of chronic glomerulonephritis do not have a previous history of acute glomerulonephritis.

Symptoms are in the form of painless hematuria and asymptomatic proteinuria (found on urine analysis). Other symptoms are seen in the form of edema of the face, eyelids, feet and legs, abdominal pain and diarrhea, general ill feeling and body ache.

Acute glomerulonephritis is characterized by oliguria or anuria, hematuria, hypertension, fluid retention, loin pain, malaise and the patient may finally develop uremia.

2. Pyelonephritis

Pyelonephritis is a kidney infection—of the pelvis and calyces—usually from bacteria that have spread from the bladder. There is fever, malaise and loin pain.

Pathophysiology This occurs due to bowel organisms that enter the urinary tract. Common organisms are *E. coli* (70 to 80%) and *E. fecalis*. Other less common organisms are coliforms and enterococci.

The most common cause is upward spread of microbes from the bladder (reflux of infected urine when bladder contracts), or from the prostate. It could also occur from infection elsewhere in the body, e.g., respiratory tract infection or a wound abscess.

There are certain virulence factors like adhesons. They are present on, essentially all, *E.coli* and have specific regions which attach to cell-receptor epitopes in a lock-and-key fashion. They lead to colonization and possibly pathogenesis of infection. But, they also get attached to polymorphonuclear leucocytes and lead to bacterial clearance.

When infection spreads into the kidney, it leads to suppuration and destruction of nephrons. Either it heals or it may proceed to chronicity causing chronic pyelonephritis.

Chronic pyelonephritis is thus an outcome of repeated attacks of acute pyelonephritis. There is scar formation. Loss of functioning nephrons finally leads to chronic renal failure and uremia. Hypertension follows.

3. Acute Renal Failure

Acute renal failure is a sudden deterioration of renal function and glomerular filtration rate, resulting in accumulation of end products of nitrogen metabolism. It is usually reversible if treated early. There is disorder of fluid and electrolyte balance.

The causes are prerenal like prolonged shock, renal like glomerulonephritis and post-renal like tumor of bladder or uterus causing obstruction to outflow of urine.

Pathophysiology Four hypotheses have been put forward:

1. Glomerular filtration occurs at a normal rate but the filtered fluid leaks back into the peritubular space due to defective tubular epithelium.
2. Intraluminal deposition of casts and cellular debris may depress glomerular filtration and lead to oliguria and renal failure.
3. There could be an altered renal hemodynamic, e.g., reduction in the renal blood flow.
4. There is probably a defect in the glomerular permeability.

4. Chronic Renal Failure

Chronic renal failure is an irreversible deterioration of kidney function where 75% of the function has been lost and the nephrons have been damaged. There is impairment of excretory, metabolic and endocrine functions of the kidney. The main causes are glomerulonephritis, hypertension, diabetes mellitus and chronic pyelonephritis. Finally, it leads to the development of uremia.

Pathophysiology The exact pathogenesis is not known.

Probably there is a suspected uremia toxin in the plasma. Probably it could be due to accumulation of certain substances in the body fluids like phosphate, urea, creatinine, guanidine, phenols and indols.

There is reduced glomerular filtration rate, selective reabsorption and secretion and glomerular fibrosis. This interferes with blood flow. This leads to uremia, polyuria, anemia, electrolyte imbalance, acidosis and hypertension.

5. Nephrotic Syndrome

Nephritic syndrome is a condition characterized by very high levels of protein in the urine called proteinuria, low levels of protein in the blood called hypoproteinemia, generalized edema, especially around the eyes, feet and hands and high blood cholesterol.

Nephrotic syndrome can occur with many diseases. In adults, the most common causes are diabetic nephropathy, glomerulonephritis, membranous nephropathy, infections and effect drugs like penicillin, and phenytoin. In older adults, the most common cause is amyloidosis. In children the cause is usually minimal-change glomerulonephritis.

Pathophysiology The permeability of glomerular capillary wall is increased due to damage to glomeruli. More proteins are presented to the tubules than can be reabsorbed. Proteins pass in the filtrate, and albumin being the smallest of the proteins, is lost in abundance. If the loss of protein exceeds the rate of hepatic synthesis, there is fall in total plasma-protein level. This leads to hypoproteinemia. There is decrease in plasma colloidal osmotic pressure. Fluid accumulates in extracellular space. This reduces the renal blood flow which stimulates the renin–angiotensin aldosterone system and hence the tubular reabsorption of sodium and water increases. This further reduces osmotic pressure and edema increases. The cycle goes on.

Plasma albumin and total plasma proteins are greatly reduced. Antithrombin is lost in urine. Hence, the incidence of atherosclerosis and thrombosis is increased.

The level of nitrogenous waste products is nearly normal. The cause of hyperlipidemia is not known.

6. Uremia

Uremia is a metabolic disorder characterized by excessive nitrogenous waste products and chiefly urea, in the blood. These are waste products of urine and due to kidney failure, are not excreted in urine and are retained in the blood.

Symptoms include anorexia, nausea, vomiting, loss of appetite and lethargy. Late symptoms include mental confusion and finally coma.

Pathophysiology There are a number of causes of uremia. Due to insufficiently operating kidneys, urea accumulates in the blood. Acute and chronic renal failure proceeds to uremia. Electrolyte imbalance is the constant feature.

7. Calculi

A calculus is a stone formed due to precipitation of mineral salts that forms in an organ or duct of a body. Formation of calculi is known as lithiasis.

The most common site for stone formation is the kidney. Stones are also formed in the gall bladder.

Stones are solid particles. In the kidney they may cause pain, nausea, vomiting, hematuria, pyuria, and possibly chills and fever. If the stone gets lodged in the ureter or passes down through it, it causes severe abdominal pain. Diagnosis is based on urinalysis and radiological imaging.

Pathophysiology Normally, salts are in solution but if urine becomes alkaline, certain types of stone formation take place.

Abnormal excess of mineral, e.g., elevated levels of calcium can cause kidney stones. Local conditions at the site can lead to stone formation, e.g., local bacteria action.

Other predisposing factors for stone formation are inactivity and prolonged bed rest, osteoporosis, parathyroid disease, gout and decreased estrogen levels in post-menopausal women.

8. Diabetic Kidney

Diabetic kidney disease is a complication that occurs in many persons with diabetes. Diabetes is the most common cause of kidney failure. Even if the diabetes is controlled, it can lead to chronic renal disease and failure.

Pathophysiology The exact cause of diabetic nephropathy is not known. But it is believed that uncontrolled high blood sugar damages the small blood vessels and the glomerulus. This occurs earlier and more commonly if there is associated high blood pressure. There is thickening and scarring of the blood vessels. These kidney structures begin to leak and protein, especially albumin, passes in urine. Damaged kidney structure leads to albuminuria.

In some cases, genes or family history may play a role. Not all persons with diabetes develop this condition.

9. Renal Hypertension

Hypertension is a major cause of kidney disease and kidney failure. For some people, hypertension is the main cause of chronic renal failure. For others, kidney disease is followed by hypertension.

Pathophysiology Hypertension causes damage to the blood vessels of the kidney. There is decreased blood supply. This stimulates the renin–angiotensin aldosterone mechanism and blood pressure is further raised. Also, as the kidneys are damaged, removal of waste and fluid is impaired. This increases fluid in the blood vessels and raises the blood pressure. The cycle goes on.

10. Tumors

Benign tumors are uncommon and mostly asymptomatic. They are discovered accidentally.

Several types of malignant tumors have been described. Renal-cell carcinoma is the most common. It is seen after the age of 50. It affects men twice as often as women. Another type is transitional cell carcinoma which affects the renal pelvis. **Wilms tumor** is one of the most common malignant tumors occurring in children.

Pathophysiology The causes of kidney cancer are not well understood. Some things have been shown to increase the risk of renal tumors. Smoking is a major risk factor. Some people have developed kidney cancer after prolonged use of painkillers called phenacitin.

Certain jobs are thought to cause kidney cancer. Those working with coke ovens and those working with asbestos have a greater risk of developing this disease.

Scientists cannot yet explain why overweight persons have more chances of getting certain types of cancer. Kidney cancer may be one of them. Maintaining an ideal weight may reduce the risk of cancer along with other diseases like heart disease, diabetes, and high blood pressure.

13.5 ARTIFICIAL KIDNEY (DIALYSIS)

13.5.1 Principle

The basic principle of the artificial kidney is to pass blood through minute blood channels bounded by a thin membrane. On the other side of the membrane is a dialyzing fluid into which unwanted substances in the blood pass by diffusion. Diffusion of solutes occurs from an area of higher concentration to an area of lower concentration through a semipermeable membrane. This is one type of artificial kidney in which blood flows continuously between two thin membranes of cellophane.

The patient's arterial blood is made to flow continuously or intermittently through the artificial kidney and then back to the body through the vein. **Heparin** is used as an anticoagulant while passing the blood through the machine. Thus, an artificial kidney is a device whereby dialysis is carried out.

The artificial kidney is used in acute renal failure, normally due to circulatory shock or mercury or other dialyzable poisonings. It is also used, some times, in chronic or permanent (end stage) renal failure.

The total amount of blood in the artificial kidney, at any one time, is usually less than 500 milliliters; the rate of flow may be several hundred milliliters per minute and total diffusion of surface area is between 0.6 and 2.5 square meters.

Also, mass transfer of solutes and water can be produced by applying a hydrostatic pressure so that fluid and solutes are forced by the process of filtration across the membranes of the dialyzer, which is called bulk flow.

13.5.2 Dialysis

In patients of uremia, when conservative treatment fails to sustain the patient, or the patient's renal status at the very time of admission is seriously impaired then it becomes necessary to go for renal replacement therapy.

1. Indications for Dialysis

(a) In Acute Renal Failure (ARF)

Biochemical Indications

(i) Blood urea > 200 mgm/dL
(ii) Serum creatinine > 10 mgm/dL
(iii) Serum K^+ > 6 meq/ L.
(iv) HCO_3 < 10 meq/L.
(v) pH < 7.2

Clinical Indications

(i) *Oliguria:* Urine formation is less than 300 mL/day
(ii) *Hyper catabolic state*
- In burns
- In crush injuries
- In septicemia

(iii) *CNS symptoms*
- Drowsiness
- Convulsions

(iv) *CVS symptoms*
- Resistant congestive cardiac failure
- Hypertensive encephalopathy
- Pericarditis
- Pulmonary edema

(v) *GIT:* Severe gastro-intestinal hemorrhage

(b) In Chronic Renal Failure (CRF)

Biochemical Indications

(i) pH < 7.2
(ii) Serum K^+ > 6 meq/L
(iii) Creatinine clearance 8 mL/min

Clinical Indications

As described in acute renal failure.

2. Types of Dialysis

Dialysis is of two types:

- Hemodialysis
- Continuous ambulatory peritoneal dialysis

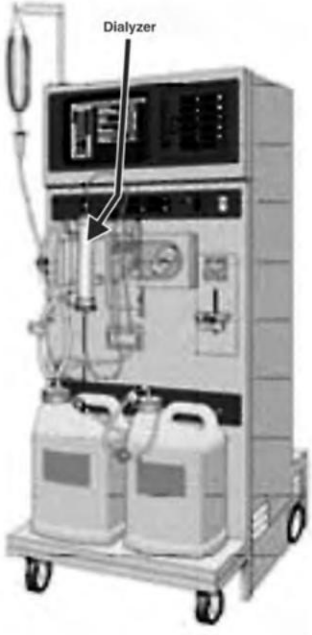


Fig. 13.6 *Dialyzer machine*

(a) Hemodialysis

The process normally requires hemoaccess, a dialyzer (dialysis machine) and dialysis solution.

It involves single passage of blood and dialysate across a semipermeable membrane.

The solutes and water move across the membrane by diffusion, to reach equilibrium.

In spite of medical treatment, when the uremia worsens, hemodialysis is started.

An arteriovenous (A-V) fistula is formed usually in the forearm. (See Fig. 13.7)

Hemodialysis is usually done 3 times weekly and each procedure lasts 3 to 5 hours.

During the first 6 weeks of treatment, uremia symptoms decrease. Though the blood urea and serum creatinine may not return to normal, many patients can lead a nearly normal life for many years.

Anemia is not corrected and osteodystrophy may worsen. (See Fig. 13.8)

Complications

The process of hemodialysis has now evolved into such a safe and efficient therapy that it can easily be performed even by the patient himself or his relative at home after a short period of training.

Still, acute or chronic complications are possible.

Acute Complications

(i) Embolism, hemolysis, clotting in the extracorporeal circulation
(ii) Hypotension during the process of dialysis, especially in elderly diabetics with autonomic neuropathy
(iii) Vomiting, headache, cramps

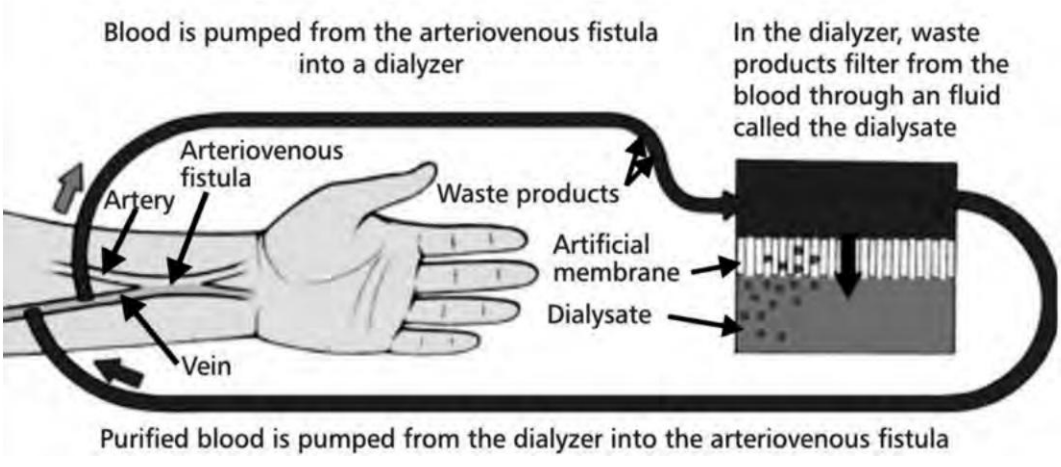


Fig. 13.7 *Process of hemodialysis*

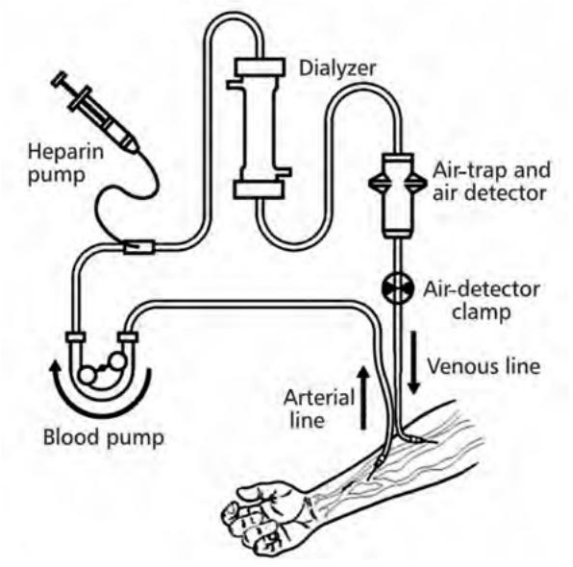


Fig. 13.8 *Apparatus for hemodialysis*

(iv) Pyrogenic reactions—uncommon
(v) Cerebral edema—headache, vomiting, drowsiness, convulsions

Chronic Complications

1. Progressive renal osteodystrophy. This occurs due to poor clearance of phosphates, abnormal vitamin D metabolism and prolonged heparin therapy.
2. Anemia of renal failure can worsen.
3. Non-A, Non-B hepatitis.
4. HIV infection is a serious threat to patients and staff.
5. Pericarditis, local amyloidosis, multicystic changes in kidneys and musculoskeletal problems.

(b) Continuous Ambulatory Peritoneal Dialysis (CAPD) An intraperitoneal catheter is introduced into the abdominal cavity and 2 liters of sterile isotonic dialysis fluid is introduced and left for 6 hours. Then it is drained and again fresh fluid is introduced.

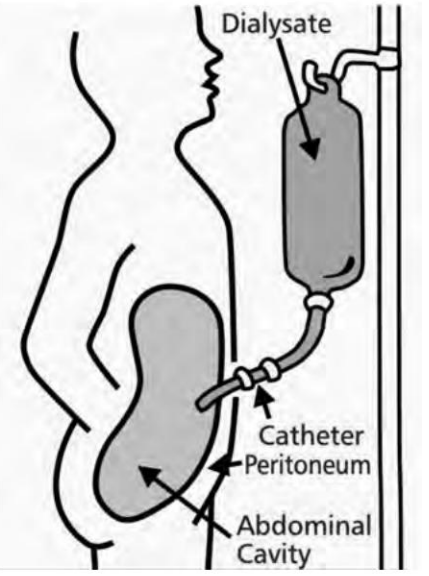


Fig. 13.9 *CAPD*

This procedure is carried out 4 times a day.

This procedure gives good result for nearly 10 years.

It is mainly done in young children and elderly patients with cardiovascular instability and patients with diabetes mellitus. (See Fig. 13.10)

Advantages

(i) Patients can be ambulatory.
(ii) Diet can be taken liberally.
(iii) Patient can lead a better quality of life.
(iv) Unstable elderly patients can easily be maintained.
(v) This procedure can be done in small children and maintained till transplant is carried out.
(vi) The patient can carry out this procedure himself at home.
(vii) Even blind patients can be trained to do this procedure themselves.

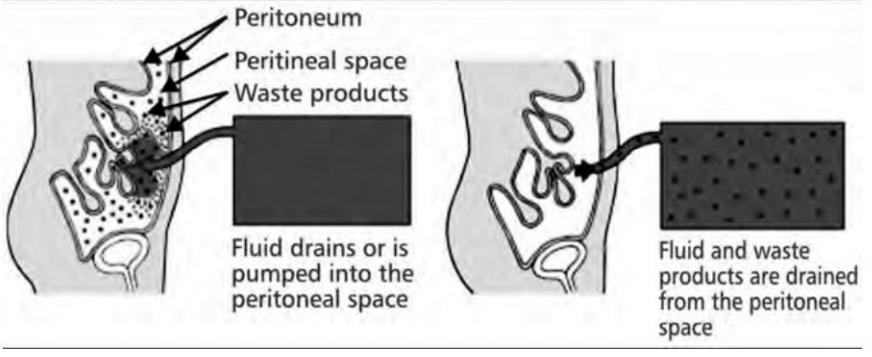


Fig. 13.10 *Peritoneal dialysis*

Complications
The main complication is peritonitis and/or recurrent peritonitis. Survival rate is 80% at 5 years.

13.5.3 Renal Transplantation

Opportunities for transplant are still limited in our country, chiefly because of shortage of donors and the high cost of immunosuppressive therapy. However, more and more specialized centers are coming up for this modality of treatment.

1. Patient Selection and Evaluation

All patients undergoing renal transplantation need to undergo extensive evaluation including detailed history, physical examination and laboratory studies.

(a) Laboratory Studies

1. Blood grouping
2. Complete hemogram
3. Liver function tests
4. Electrolytes
5. Human Leukocyte Antigen (HLA) typing
6. Lipid profile
7. Serum proteins
8. Hepatitis B profile
9. Viral titers
10. ECG
11. Upper GI endoscopy

(b) Radiological Studies

1. Chest X-ray
2. Voiding cystourethrogram
3. Cardiac catheterization

(c) Donor

1. Living, related donor
2. Living, unrelated donor
3. Cadaver donor

The best results are obtained with a living, related donor.

Advantages of a living, related donor are

- Better HLA match
- Optimum preparation of recipient
- Planned operations under ideal conditions

(i) Evaluation of Donor All the laboratory procedures done in the patient have to be carried out in the donor also.

Besides these, the following other investigations are also done.

- GTT: Glucose Tolerance Test
- HIV status
- Pregnancy test for females
- Radiological studies
- X-ray chest
- $^{1}/_{V}$ pyelogram

(ii) Contraindications to Donation

1. Advanced age > 65 years
2. Diabetes mellitus
3. Hypertension
4. Any other medical illness

Unrelated, living donors are usually discouraged for donating.

(iii) Cadaver Donors Usually, those who have died in accidents by head injury are selected and they should fulfill the criteria for brain death, viz.,

1. Hypothermia
2. Comatose patient on ventilator
3. Apnea
4. Absent brain-stem reflexes
5. Positive diagnosis of coma
6. EEG

2. Post-operative Care

After the renal transplant is carried out, the patient is kept under barrier nursing in an isolated room for at least one week after surgery. Vital signs, fluid and electrolyte status are carefully monitored.

Urine output is replaced milliliter to milliliter in the first 24 hours.

Volume replacement is gradually decreased after the first 24 to 48 hours and clear liquid diet is started on the second post-operative day.

3. Immunosuppression

Long-term therapy with immunosuppressive agents is necessary.

(a) Prednisolone
(b) Cyclosporin
(c) Azathioprine

Immunosuppression is associated with increased incidence of infections, especially opportunistic infections and there is increased incidence of skin neoplasm.

4. Contraindications to Renal Transplantation

(a) Absolute Contra–indications

1. Active infection
2. HIV positive
3. Disseminated malignancy
4. Drug abuse
5. Uncontrolled psychosis
6. Advanced cardiovascular, liver or respiratory failure
7. Severe congenital urinary tract abnormality

8. Oxalosis
9. Fabry's disease

(b) Relative Contraindications

1. Age less than 5 years and more than 60 years
2. Medical noncompliance
3. Active peptic ulcer disease
4. Severe secondary hyperparathyroidism
5. Renal disease with a high recurrence rate

5. Rejection

Four clinical forms of human renal allograft rejection are recognized, viz.,

1. Hyper acute rejection
2. Accelerated acute rejection
3. Acute rejection
4. Chronic rejection

6. Complications

(a) Vascular, viz., renal artery thrombosis and hemorrhage

(b) Urologic, viz., urinary leak, vesicoureteric reflux, urinary tract infection

(c) Lymphatic, viz., lymphocoele

(d) Infections are the most important cause of morbidity and mortality after transplantation; careful measures have decreased this incidence

(e) Malignancy develops in 5 to 6%

(f)
- Cardiovascular disease accounts for 20 to 30% of death in these patients especially in elderly and diabetics.
- Hypertension occurs in 80% in post-operative period.
- Hyperlipidemia

(g) Diabetes mellitus

(h) Gastrointestinal diseases like acute pancreatitis, ulcers colitis, and diverticulitis

(i) Miscellaneous, viz., metabolic, hematogenic recurrent renal disease, etc.

REVIEW QUESTIONS

1. Describe the general features of the kidney. What are its functions?
2. Write a note on the structural and functional unit of the kidney (nephron). Describe the physiology of urine formation. Describe in detail the counter-current mechanism of urine formation.
3. What is GFR? Describe the factors that regulate GFR.
4. Write a note on the structure and location of the urinary bladder.
5. Describe the different parts of the male urethra.
6. Discuss the physiology of micturition.
7. Describe the evaluation of renal function by examination of blood and urine.
8. Describe the concentration and dilution of urine.
9. Write about kidney function tests.
10. Write a note on disorders of the kidney with the pathophysiology.
11. Write short notes on:
    a. Hemodialysis
    b. Peritoneal dialysis
    c. Nephron
    d. Bowman's capsule
    e. Glomerular apparatus
    f. Juxtaglomerular apparatus
    g. GFR
    h. Renal blood-flow measurement
    i. Kidney transplant
    j. Acute renal failure
    k. Chronic renal failure

Chapter

14 Integumentary System

- **SKIN**
  - **Structure**
    - **Epidermis**
      - **Cells**
        - **Keratinocytes**
        - **Melanocytes**
        - **Merkel cells**
        - **Melanocytes**
      - **Strata**
        - **Stratum basale**
        - **Stratum spinosum**
        - **Stratum granulosum**
        - **Stratum lucidum**
        - **Stratum corneum**
    - **Dermis**
      - **Papillary layer**
      - **Reticular layer**
    - **Hypodermis**
  - **Functions**
  - **Applied physiology**
    - **Regulation of body temperature**
      - **Heat production**
      - **Heat loss**
        - **Radiation, conduction, convection and evaporation**
      - **Other factors affecting temperature**
        - **Sweat glands**
        - **Blood flow in the dermis**
  - **Skin disorders**
    - **Eczema**
    - **Psoriasis**
    - **Acne**
    - **Urticaria**
    - **Seborrheic dermatitis**
    - **Angioneurotic edema**
    - **Scabies**
    - **Pruritus**
    - **Warts**
    - **Ringworms**

Introduction

The integumentary system consists of the skin, hair, nails, subcutaneous (below the skin) tissue, muscles, nerves and assorted glands. The function of the integumentary system is to protect the body, to maintain the body temperature and to give sensory information about the surrounding environment.

The **skin** not only keeps harmful substances away from the inner structures, but also prevents the loss of fluids from within.

The **hair** on the scalp provides insulation from cold for the head. The hair of eyelashes and eyebrows helps keep dust and perspiration out of the eyes, and the hair in the nostrils helps keep dust out of the nasal cavities. Any other hair on our body no longer serves a function, but is an evolutionary remnant.

Nails protect the tips of fingers and toes from mechanical injury, and enhance sensation of the fingertip. They also help fingers in their finer actions, e.g., picking up the small objects.

Subcutaneous tissue connects the skin to underlying tissues such as muscles. Fat contents of the subcutaneous tissue provide insulation to the body.

Glands in the integumentary system are of four types:

1. **Sudoriferous glands**—They are sweat-producing glands. They help maintain body temperature.
2. **Sebaceous glands**—They are found in the skin except in the palms of the hands and soles of the feet. They secrete an oily substance called sebum. **Sebum** is odorless, but bacterial breakdown can produce odors. Sebum is the cause of 'oily' hair, if it is not washed for several days. It helps inhibit bacteria, keep the skin waterproof and prevents drying of hair and skin.
3. **Ceruminous glands**—They produce cerumen (earwax), secreted in the ear canal, which keeps the outer surfaces of the eardrums clean, soft and prevents drying by its lubricating action. It also has antibacterial and antifungal role.
4. **Mammary glands**—They produce milk and is discussed in the appropriate chapter.

14.1 SKIN

The skin is made up of layers of tissue that guard underlying muscles and organs. It plays the most important role of protection against pathogens. Its other main functions are to provide insulation to the underlying structures, to regulate the body temperature, to provide the perception of sensation and to help in synthesis of vitamins B and D.

The skin is often known as 'the largest organ in the human body' with regards to surface area and weight. It covers the body. It weighs more than any single internal organ, accounting for about 15 per cent of body weight. For the average adult human, the skin has a surface area of between 1.5–2.0 square meters; most of it is between 2–3 mm thick. The average square inch of skin holds 650 sweat glands, 20 blood vessels, 60,000 melanocytes, and more than a thousand nerve endings.

Damaged skin will try to heal by forming scar tissue, often giving rise to discoloration and depigmentation of the skin.

14.1.1 Structure

The skin has two major layers which are made of different tissues, each of them having different functions. They are the epidermis and the dermis. Below these layers lies the hypodermis or subcutaneous adipose layer, which is not usually classified as a layer of skin.

1. Epidermis

The outermost layer, i.e., the epidermis, consists of stratified squamous keratinizing epithelium with an underlying basement membrane. It contains no blood vessels and is nourished by diffusion from the dermis. The main types of cells which make up the epidermis are keratinocytes, melanocytes, Merkel cells and Langerhans cells.

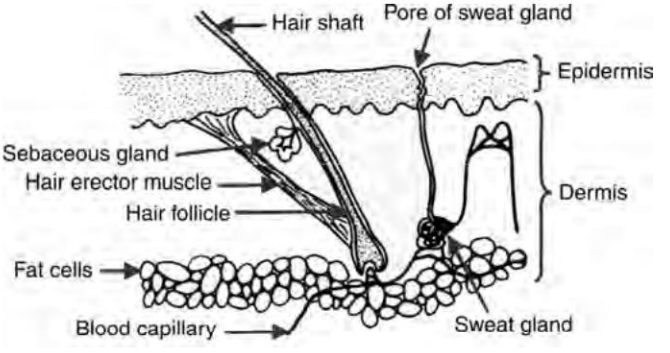


Fig. 14.1 *Skin—cross section*

90% of epidermal cells are **keratinocytes** which produce a tough, fibrous protein called **keratin**. Keratinocytes are arranged in four to five layers, which protect underlying structures from chemicals, microbes and heat.

Melanocytes produce the pigment **melanin**. The slender projections of melanocytes extend between the keratinocytes and transfer melanin granules to them. Melanin is a brown–black pigment and is responsible for the color of the skin. Human-skin pigmentation varies among populations in a striking manner. This has led to the classification of people on the basis of skin color. Melanin absorbs some of the potentially dangerous radiation in sunlight. It also contains DNA repair enzymes which reverse UV (ultraviolet) damage. People who

lack the genes for these enzymes suffer high rates of skin cancer called malignant melanoma, which is particularly invasive, spreads quickly, and can often be deadly.

Langerhans cells form a small fraction of the epidermis. They are formed in the bone marrow and come to the epidermis. They are damaged by UV light. They protect against microbes.

Merkel cells form a very small fraction of the epidermis. They lie deeply and are in contact with Merkel's disk, and together they detect different touch sensations.

The epidermis can be further subdivided into the following **strata** (beginning with the innermost layer): basale, spinosum, granulosum, lucidum and corneum. Cells are formed through mitosis at the innermost layers. They move up the strata, changing shape and composition and eventually reach the corneum and become sloughed off (desquamation). This process is called **keratinization**, which takes place within about 30 days.

- **Stratum basale** is the deepest layer and consists of a single layer of keratinocytes. This layer protects the deeper layers from injury.
- **Stratum spinosum** is superficial to stratum basale. There are 8 to 10 layers of closely packed keratinocytes. This layer gives strength and flexibility to the skin.
- **Stratum granulosum** is the middle layer and consists of 3 to 5 layers of keratinocytes. It marks the transition between the deeper and superficial layers. In the keratinocytes, lamellar granules are present, which release a lipid-rich secretion.
- **Stratum lucidum** is seen only in the thick skin of fingertips, palms and soles. It consists of 3 to 5 layers of dead keratinocytes with a large amount of keratin.
- **Stratum corneum** consists of nearly 25 to 30 layers of dead keratinocytes. It helps to protect deeper layers from microbes and injury.

Epidermis is responsible for keeping water in the body and keeping other harmful chemicals and pathogens out.

Blood capillaries are found beneath the epidermis and are linked to an arteriole and a venule.

2. *Dermis*

The dermis lies below the epidermis and contains a number of structures including blood vessels, nerves, hair follicles, smooth muscle, glands and lymphatic tissue. The main cell types are fibroblasts, adipocytes (fat cells) and macrophages. It consists of loose connective tissue, called areolar connective tissue, consisting of collagen, elastin and reticular fibers. It can be split into the papillary and reticular layers.

The **papillary layer** is superficial and extends into the epidermis. It is composed of loosely arranged fibers containing elastic fibers. Free nerve endings are also present in this layer which is responsible for sensations of pain, temperature,

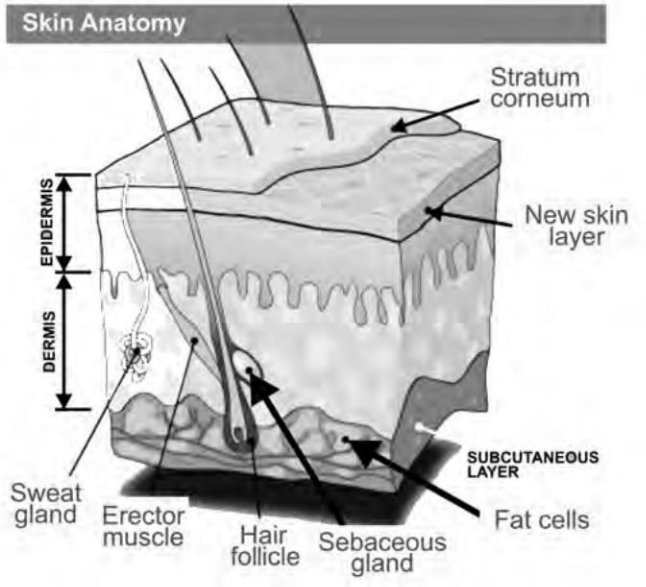


Fig. 14.2 *Schematic section of skin*

itching and tickling. Papillary ridges make up the lines of the hands giving us fingerprints. They are also seen on the surfaces of soles and toes. They appear as straight lines or form loops and whorls.

The **reticular layer** is denser and is continuous with the hypodermis. It contains the bulk of the structures (such as sweat glands). It is composed of irregularly arranged collagen bundles and coarse elastic fibers. Hence, it gives the skin strength, elasticity and extensibility.

Erector muscles, attached between the hair papilla and epidermis, when contract, pull the hair fibers and produce goose bumps. Sweat glands open up via a duct onto the skin by a pore. Sebaceous glands are exocrine glands which produce a mixture of lipids and waxy substances, viz., sebum. Sebum performs the function of lubrication and waterproofing and also has an antibactericidal action.

3. *Hypodermis*

It lies below the dermis and is not a part of the skin. Its purpose is to attach the skin to underlying bone and muscle as well as supply it with blood vessels and nerves. It consists of loose connective tissue and elastin. The main cell types in this layer are fibroblasts, macrophages and adipocytes (the hypodermis contains 50% of body fat).

14.1.2 Functions

1. **Protection**—Skin gives an anatomical barrier between the internal and external environment in bodily defense. Langerhans cells are part of the immune system. Macrophages in the dermis phagocytize bacteria. Keratin protects underlying tissues from microbes, heat, chemicals

and injury. Sebum protects the skin from becoming dry. Lipids which are released from the lamellar granules perform a very important protective function. They retard evaporation of water from the surface of the skin. They also retard the entry of water into the skin, e.g., during bathing, and thus the combined effect is prevention of dehydration. Melanin helps in protection against the damaging effect of UV light. Perspiration is acidic and retards growth of some microbes.

2. **Sensation**—Skin reacts to heat, cold, touch, pressure, vibration, and tissue injury. Sensations arise in the skin. There are nerve endings, tactile receptors in the epidermis and touch corpuscles in the dermis. There are also hair-root plexuses around the hairs. These all are responsible for the perception of sensations.
3. **Heat Regulation**—The skin has a blood supply far greater than its requirements. This allows control of energy loss. Dilated blood vessels increase perfusion and heat loss while constricted vessels greatly reduce cutaneous blood flow and conserve heat. Erector muscles, under the control of the autonomic nervous system, contract, relax or shiver. Thus, the skin retains or loses the heat which helps in maintaining the body temperature. Sweat also plays an important role in heat regulation. When there is high environmental temperature, there is evaporation of sweat from the skin surface and temperature is lowered. With low environmental temperature, sweat production decreases and heat is conserved.

   Hairs also serve as an insulator of heat. Fat and subcutis serve as a nonconducting pad and thus preserve heat.
4. **Vitamin D Synthesis**—UV rays of sunlight activate a precursor molecule in the skin. The activated molecule is modified in the kidneys and liver. Calcitriol is produced which helps in the absorption of calcium.
5. **Absorption and Excretion**. Certain lipid-soluble materials are absorbed through skin, e.g., fat-soluble vitamins and certain drugs. Certain topical steroids are lipid soluble and are absorbed through the skin and thus exert an anti-inflammatory action by inhibiting production of histamine by mast cells. Excretory function of the skin is minimal. Sweat plays this role. About 200 mL of water is lost through sweat every day. Small amounts of salts, urea and ammonia are also lost through sweat.
6. **Storage**—The skin stores many substances like water, salt (sodium chloride), fats and glucose.

14.1.3 Applied Physiology

The transdermal patch is an increasingly popular drug-delivery system. These patches are designed in such a way that the drug molecules diffuse through the epidermis to the blood vessels in the dermis layer. A typical patch works well for small lipid-soluble molecules, e.g., estrogen, nitroglycerin, and nicotine.

1. Regulation of Body Temperature

Body temperature is maintained when the amount of heat lost and the amount of heat produced are nearly equal. This process is one aspect of homeostasis. The normal temperature of the body is 36.8°C (98.4°F).

The temperature of the body is regulated by neural feedback mechanisms which operate through the hypothalamus. Impulses are received from the thermoreceptors in the skin and are sent to the heat losing and heat-promoting centers in the hypothalamus, which in turn respond by lowering or raising the body temperature respectively.

2. Heat Production

Certain factors are responsible for heat production:

- Metabolic rate affects heat production.
- Metabolic rate of a child is more as compared to older persons.
- Metabolic rate is lower in females as compared to males.
- Metabolic rate is also lower during sleep.
- Contraction of skeletal muscles produces heat. The more strenuous the contraction, the greater the heat produced.
- Shivering increases heat production.
- Secretion of norepinephrine, epinephrine (by increasing the metabolic rate of body cells) and thyroxine (by increasing the basal metabolic rate) increases heat production.
- Food ingestion raises the metabolic rate. During peristalsis and during digestion, heat is produced by chemical reaction.
- Heat is produced as a by-product by the liver during its activity.

3. Heat Loss

Heat is lost from the body mainly through the skin. Some amount of loss is through urine, feces and expired air.

The heat transfer mechanisms are radiation, conduction and convection, and evaporation.

In **radiation,** the exposed parts of the body lose heat by radiating more infrared rays.

In **conduction,** heat is lost by conduction to those objects in contact with the skin, e.g., clothes, jewellery, etc. (Heat can also be gained by conduction, e.g., while taking a bath in a bathtub, heat is gained by conduction.)

When air passes over the body, it gets warm, rises up and gets replaced by cool air. This sets up **convection** currents. Heat is also lost from clothes in this way. Rate of convection is faster when movement of air is faster.

Evaporation occurs through skin and expired air. This is also called insensible loss. Humidity affects evaporation. Higher the humidity, greater the evaporation.

4. Other Factors Affecting Temperature

(a) Sweat Glands When body temperature increases, sweat glands are stimulated to secrete sweat which comes on the surface of the skin, gets evaporated and brings the temperature down.

(b) Blood Flow in the Dermis When external temperature is low, sympathetic nerves stimulate the blood vessels in the dermis causing vasoconstriction and heat is conserved due to less blood flow. Arterioles get dilated when heat production increases. There is increase in blood flow and heat is lost.

In fever, heat loss mechanisms get activated and there is profuse sweating and vasodilatation.

Thus, homeostasis is maintained and a balance is maintained between heat produced in the body and heat lost to the exterior.

14.2 SKIN DISORDERS

1. Eczema

Eczema is a general term for a rashlike skin condition. It is a chronic superficial inflammation of the skin where the skin becomes red and inflamed. There are small vesicles which could be dry or wet. The dry variety forms crusts and scales. The wet variety oozes and then dries. The most common type is **atopic dermatitis**.

Pathophysiology The exact cause is not known. It is an allergic reaction to some irritant. It occurs in adults and children but is most common in babies.

Family history sometimes plays a role.

2. Psoriasis

Psoriasis is a common chronic condition characterized by flaky white patches and plaques, and dry well-circumscribed scaly papules which are of different sizes.

Pathophysiology Psoriasis is an auto-immune condition. The immune system protects the body against infection and disease by attacking bacteria and viruses. When there is psoriasis, T-cells, a kind of white blood cells that are a part of the immune system, attack the skin cells mistakenly. The body then produces other immune responses, leading to swelling and rapid production of skin cells.

Psoriasis is connected to family history.

Certain conditions can cause psoriasis to worsen—stress, infections like sore throat, diseases that weaken the immune system, skin irritation, cold weather, smoking and certain medicines like beta-blockers.

3. Acne

Acne (*acne vulgaris*) is a common skin disease characterized by areas of multiple non-inflammatory follicular papules, inflammatory papules (sterile as they do not contain bacteria), pustules and nodules in its more severe forms. The lesions are referred to as pimples, blemishes, spots or simply acne. Severe acne is inflammatory.

Pathophysiology Acne occurs most commonly during adolescence. This is due to an increase in male sex hormones when both males and females enter puberty. Usually, it disappears in the early twenties, but in some individuals it may last longer.

Acne occurs mostly in the areas of skin with the densest population of sebaceous follicles. These areas are the face, upper part of chest, shoulder and back. Lesions are caused by changes in pilosebaceous units, skin structures consisting of a hair follicle and an associated sebaceous gland. Changes are caused by androgen stimulation.

4. Urticaria

Urticaria is an allergic skin rash characterized by erythema and local wheal formation.

There are three types of urticaria:

- *Acute urticaria*—lasts for several hours to six weeks
- *Chronic urticaria*—persists for more than six weeks
- *Physical urticaria*—lasts for an hour or two

Pathophysiology Acute urticaria is caused by an allergy to pets, latex, food, medicines like antibiotics and aspirin and wasp stings.

Viral infections such as glandular fever, dental infections, fungal infections, blood transfusions and vaccines can cause acute urticaria.

The exact cause of chronic urticaria is not known. Probably it is caused by the body's development of antibodies to itself, called auto-antibodies.

Chronic bacterial and parasitic infections, thyroid disease, auto-immune diseases and long-term use of antihypertensives can cause chronic urticaria.

Chronic urticaria is often accompanied by coexistent physical urticaria triggered by environmental exposure to heat, cold, sunlight, or due to pressure on the skin.

5. Seborrheic Dermatitis

Seborrheic dermatitis is a papulosquamous scaling disorder seen on the scalp, face and trunk. The severity varies from mild dandruff to exfoliative erythroderma.

Pathophysiology Seborrheic dermatitis is associated with normal levels of malassezia but an abnormal immune response and activation of complement. Helper T cells and antibody titers are depressed. Malassezia releases inflammatory free fatty acids and activates the alternative complement pathway.

It is commonly aggravated by changes in humidity and seasons, scratching or emotional stress.

6. Angioneurotic Edema

Angioneurotic edema is a syndrome where there are recurrent episodes of non-inflammatory swelling of the skin, mucous membrane, viscera, brain and intestinal organs accompanied by arthralgia, purpura and fever. In severe cases, respiratory swelling can result in compromised breathing.

Pathophysiology Angioneurotic edema is often caused by an allergic-type reaction. It occurs because histamine is released from the mast cells which leads to a chain of events resulting in allergy and angioedema.

There are certain triggering factors—pollen, foods, stress, drugs (ACE inhibitors), insect bites, corticosteroids, antihistamines, exposure to cold, heat, water or sunlight, and also after infection.

7. Scabies

Scabies is an itchy, highly contagious parasitic infection that causes small bumpy rashes and blisters. There appear short, reddish, or darkened lines on the skin surface, especially around the wrist and between the fingers.

Pathophysiology Scabies is caused by the itch mite. Scabies mites are very sensitive to their environment. They burrow into the top layer of the skin to lay their eggs. Direct skin-to-skin contact is the mode of transmission. Sexual contact is one of the most common modes of transmitting the disease. The infection spreads more easily in crowded conditions and in schools.

8. Pruritus

Pruritus is a common manifestation of dermatological diseases like atopic dermatitis, xerotic eczema and allergic contact dermatitis. The symptom increases with age. In some, the condition may be so severe that it affects sleep and quality of life.

Pathophysiology A single mechanism cannot explain all causes of pruritus.

Histamine is released by mast cells in persons with urticaria and allergic reactions and is probably associated with pruritus. With the exception of allergic conditions, histamine must be considered only one of the chemical mediators of itch.

Pruritus originates within the skin's nerve endings and are transmitted through C fibers to the dorsal horn of the spinal cord and then to the cerebral cortex via the spinothalamic tract and generates a reflex, the scratch.

While it occurs most commonly in skin disorders, it may be an important dermatological clue to an underlying systemic disease.

Serotonin appears to be a key component of the pruritus that occurs with several diseases like polycythemia vera, uremia, cholestasis and lymphoma. Serotonin inhibitors like cyproheptidine and paroxetine have proved effective in treating several of these pruritic conditions.

Regardless of the cause, pruritus often is exacerbated by a dry or hot environment, stress and skin inflammation.

9. Warts

A wart is a small, rough, benign, epithelial tumor seen on the hands and feet. The appearance differs based on the type of wart and where it is located. Most are well defined with thickening of the skin.

Pathophysiology Warts are caused by the human papilloma virus. They are contagious by contact. They are common in children from 12 to 16 years and usually disappear without treatment within 3 years.

10. Ringworm

Ringworm is a fungal infection in the skin caused by several different kinds of fungi. The rashes are either dry or scaly or wet and crusty. Appearance is a ring-shaped rash that is reddish and may be itchy. It occurs on the scalp, neck, axilla, under the breasts and in the groin.

Pathophysiology It is caused by different fungi. It is transmitted from direct contact with an infected person or an infected animal.

REVIEW QUESTIONS

1. Describe structure and functions of the skin.
2. Describe the regulation of body temperature in detail.
3. Describe the various disorders of the skin.
4. Write short notes on:
   a. Dermis
   b. Epidermis
   c. Functions of the skin

Chapter

15 Blood

- **BLOOD**
  - **Composition**
    - **Cells**
    - **Plasma**
      - **Organic substances**
      - **Inorganic substances**
  - **Properties of blood**
  - **Functions of blood**
- **BLOOD VOLUME**
- **PLASMA PROTEINS**
- **RED BLOOD CELLS**
  - **Erythropoiesis**
    - **Maturation**
    - **Regulation**
  - **Fate**
  - **Properties**
  - **Functions**
  - **ESR**
    - **Determination**
      - **Westergren's Method**
      - **Wintrobe's Method**
    - **Normal values**
  - **Hemoglobin**
    - **Normal values**
    - **Synthesis**
    - **Properties**
    - **Functions**
    - **Estimation**
- **WHITE BLOOD CELLS**
  - **Formation or synthesis**
    - **Granulocytes**
    - **Lymphocytes**
    - **Monocytes**

- Morphology ..... Neutrophils
  - ..... Eosinophils
  - ..... Basophils
  - ..... Monocytes
  - ..... Lymphocytes
- Functions
- Variations ..... Physiological, Pathological

• PLATELETS

- Formation
- Structure
- Functions
- Variations ..... Physiological, Pathological variations

• COAGULATION OF BLOOD

• BLOOD GROUPS

- ABO blood grouping system
- Rh (Rhesus) factor blood grouping-system
- Determination ..... Universal donor
  - ..... Universal recipient

• BLOOD TRANSFUSION

- Indications
- Types
- Complications..... Transfusion reactions
  - ..... Transmission of disease

• DISORDERS OF RBC

- ..... Anemia
  - Classification..... Deficiency
    - ..... Blood destruction
    - ..... Hypoplasia or aplasia
    - ..... Hereditary
  - ..... Iron-deficiency anemia
  - ..... Megaloblastic anemia
  - ..... Haemolytic anemia
  - ..... Aplastic anemia
  - ..... Sickle-cell anemia
  - ..... Thalassemia

- **DISORDERS OF WBC**
  - Leucopenia
  - Leucocytosis
  - Monocytosis
  - Lymphocytosis
  - Leukemia ..... Acute leukemia
- **DISORDERS OF PLATELETS**
  - Thrombocytopenia
  - Thrombocytosis
  - Thrombocythemia
- **DISORDERS OF COAGULATION**
  - Disseminated intravascular coagulation (DIC)
  - Hemophilia
  - Von Willebrand's disease

Introduction

Blood is a body fluid that carries necessary substances to the body's cells—oxygen and various nutrients—and transports waste products away from those same cells. It circulates in the body by the pumping action of the heart.

15.1 BLOOD—COMPOSITION, PROPERTIES AND FUNCTIONS

15.1.1 Composition of Blood

Blood is composed of blood cells which are suspended in a liquid called plasma.

Cells constitute 45% of blood. The cells are red blood cells, white blood cells and platelets.

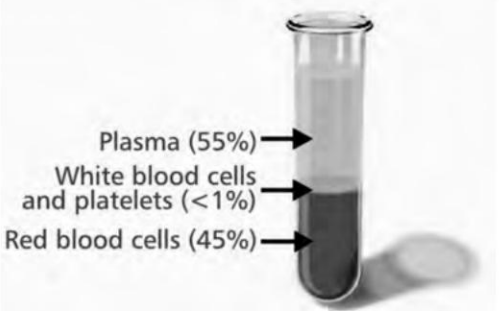


Fig. 15.1 *Composition of blood*

Plasma is the noncellular part of blood. It comprises 55% of blood and is mostly water (90% by volume). It is light cream in color. It communicates continuously with the interstitial fluid through the pores of the capillary membranes, which are highly permeable to almost all solutes except the proteins. Hence, the extracellular fluids are constantly mixing, so that plasma and interstitial fluids have about the same composition except for proteins.

It contains organic and inorganic substances and the cellular elements.

Organic Substances are dissolved proteins, glucose, fats, nonprotein nitrogenous substances like ammonia and amino acids, hormones, antibodies like immunoglobulin, coloring pigments like bile pigments and enzymes.

Inorganic Substances are mineral ions like sodium, potassium, calcium, etc. Oxygen and carbon dioxide are the gases present in plasma.

15.1.2 Properties of Blood

Blood amounts to about 5 liters in an adult human and accounts for 8% of the body weight. Its normal pH range is 7.35–7.45, i.e., it is slightly alkaline in nature.

It is red in color and is opaque. Arterial blood is scarlet red and venous blood is purple red.

Specific gravity of total blood is 1.052 to 1.061, that of blood cells is 1.092 to 1.101 and of plasma is 1.022 to 1.026.

Blood is five times more viscous than water. This is chiefly due to red blood cells and plasma proteins.

15.1.3 Functions of Blood

The human body consists of metabolically active cells that need a continuous supply of nutrients and oxygen. Blood is the primary transport medium that is responsible for meeting these cellular demands.

(a) Transport of Nutrition Nutritive substances like glucose, amino acids, lipids and vitamins are derived from the digested food. They are absorbed from the gastrointestinal tract and carried, by blood, to the different parts of the body for growth and energy.

Due to various metabolic reactions, waste products are released in the tissues and these are removed by blood and carried to the organs of excretion like kidneys, skin, liver, etc.

(b) Maintenance of Fluid and Electrolyte Balance The water content of blood is freely interchangeable with interstitial fluid and thus, helps in the regulation of water content of the body. When necessary, adjustments are made by decreasing or increasing the amount of water lost in urine and in perspiration.

(c) Regulation of Acid–Base Balance Plasma proteins and hemoglobin act as buffers and help in regulation of acid–base balance. They prevent shift of pH in the blood. Various ions are excreted through kidneys, lungs and skin to restore normal pH whenever it gets altered.

(d) Regulation of Body Temperature Blood helps to regulate the body temperature. The balance between heat loss and heat gain is maintained by blood.

(e) Functions as a Vehicle or Transport Agent Hormones and some enzymes are carried by blood from their place of secretion to the necessary parts of the body, where they have to carry out their function.

(f) Transport of Gases Respiratory gases are transported by the blood. Oxygen, which is required by all the cells and tissues for their metabolic activities, is carried from the alveoli of the lungs to the different parts of the body and supplied to

the cells, and carbon dioxide is taken away from the cells to the alveoli of the lungs.

(g) Storage Function Blood contains glucose, proteins, water, sodium, potassium, etc., which are constantly required by the tissue. Whenever conditions like fluid loss or electrolyte loss occurs, e.g., during diarrhea, vomiting or starvation then blood serves as a good source for supplying these substances.

(h) Body Defense The leucocytes present in the blood play an important role in the defense of the body.

- **Neutrophils and monocytes** engulf bacteria and foreign particles by phagocytosis.
- **Lymphocytes** are involved in immunity.
- **Eosinophils** are responsible for detoxification, disintegration and removal of foreign proteins.
- **Clotting mechanisms** prevent blood loss, and thereby fluid loss through hemorrhage, when blood vessels become damaged.
- **Antibodies** in the plasma help protect against disease by their reactions with offending agents.

15.2 BLOOD VOLUME

Blood volume is the volume of blood in the circulatory system. An adult human has a blood volume of about 5 liters. Normally, the blood volume is maintained within the normal range by the amount of water and sodium ingested, water and sodium excreted by the kidneys in urine and to some extent from the lungs, skin and gastrointestinal tract.

Regulation of blood volume is affected by hormonal influences and nervous reflexes. It regulates the amount of water and sodium excretion by the kidneys. For example, if more water and sodium are ingested, the kidneys respond by excreting more water and sodium in the urine. It is also affected by the mechanism of fluid exchange that is taking place at the capillaries. Blood pressure, osmosis and diffusion also play a role in regulation of blood volume. Natural forces like sweating and thirst affect blood volume.

Blood volume can be measured by using substances that combine with red blood cells—iron, phosphate or chromium, or substances that combine with plasma proteins.

Measurement of blood volume is based on the dilution principle—the volume of any fluid compartment can be measured if a given amount of a substance is dispersed in the fluid within the compartment and the extent of dilution is then measured.

There are normal physiological variations seen in blood volume.

- Blood volume is more in males.
- In women, blood volume increases during pregnancy.
- It increases during exercise probably due to splenic contraction.
- Anoxia increases blood volume. Hence, there is increased blood volume at higher altitudes.

15.3 PLASMA PROTEINS

Blood proteins, or serum proteins, are important constituents found in blood plasma. The amount of total serum proteins in blood is 7 g/dL, which in total makes 7% of the total blood volume. The plasma proteins are albumin, globulin and fibrinogen. All the plasma proteins are synthesized in the liver except gamma globulins, which are synthesized from lymphocytes.

Table 15.1 *Important blood proteins*

Name	*%*	*Function*
Albumin	60%	Creates osmotic pressure and transports other molecules
Immunoglobulins	35%	Participate in immune system
Fibrinogen	4%	Blood coagulation
Alpha 1-antitrypsin		Neutralize trypsin that has leaked from the digestive system
Regulatory proteins	<1%	Regulation of gene expression

15.3.1 Functions

60% of plasma proteins are made up of the protein **albumin,** which plays a major role in maintaining the osmotic pressure of plasma, thereby regulating the blood volume.

Globulins make up 35% of plasma proteins. They are necessary for the manufacture of immune substances like antibodies, bacteriolysins and agglutinins.

4% is **fibrinogen.** It is essential in the clotting of blood and can be converted into insoluble fibrin.

Regulatory proteins which make up less than 1% of plasma proteins are proteins such as enzymes, proenzymes and hormones.

Plasma proteins assist in the transport of lipids, ions and hormones.

They give viscosity to blood and hence, blood pressure is maintained.

Plasma proteins have the property of binding to certain drugs. This combination is inactive and not excreted. Also, adverse drug reactions are possible due to binding of plasma proteins to drugs.

Separating serum proteins by electrophoresis helps in valuable diagnosis, and repeated screening helps in monitoring the clinical progress.

15.4 RED BLOOD CELLS (ERYTHROCYTES)

Red blood cells are the most common type of blood cells, and their principal function is to deliver oxygen to the body tissues via the blood. The cells contain hemoglobin and the red color of blood is attributed to it. They take up oxygen in the lungs and release it while squeezing through the body's capillaries at the tissue level. They develop in the bone marrow and their life span is about 120 days.

(a) Normal Value In adult males, it is 5 m/cu mm of blood and in adult females, 4.5 m/cu mm of blood.

(b) Normal Size Each cell has a mean diameter of 7.8 micrometers. It is **t**hicker at the periphery, thickness being 2.2 u, and thinner at the center, thickness being 1 u.

Red blood cells, when of small size, are called **microcytes**. They are seen in iron-deficiency anemia. **Macrocytes** are the red blood cells with a bigger size and are present in the blood in megablastic anemia.

Anisocytes are the red blood cells of unequal size and are seen in the blood in pernicious anemia.

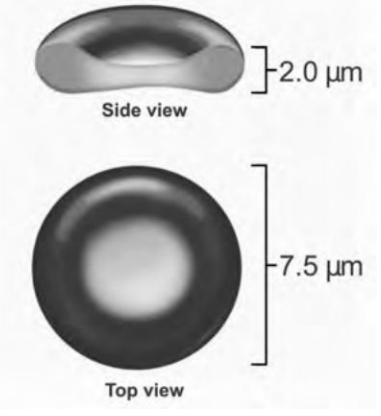


Fig. 15.2 *Red blood cells*

The red blood cells are biconcave (dumb-bell shaped) in **shape**. The biconcave shape helps in rapid diffusion of oxygen and other substances into the interior of the cell. It also provides large surface area for removal or absorption of substances. Because of their sleek shape, they can squeeze through capillaries very easily which helps in perfusion.

Abnormal shapes of red blood cells occur in different types of anemia. They could be spherocytes, elliptocytes, crescent-shaped (called sickle cell), or they could be crenated (shrunk). Unequal-shaped cells due to deformed cell membranes are called **poikilocytes**, and these could be flask-shaped, hammer-shaped or of some unusual shape.

Packed cell volume is the volume of red cells in 1 liter of whole blood.

Mean cell volume is the average volume of cells.

15.4.1 Erythropoiesis

Erythropoiesis is the process by which red blood cells are produced in the red bone marrow. Up to five years of age, all bones produce RBC. By the age of 25 years, the tibia and femur stop formation, while vertebrae, sternum, pelvis, proximal limb bones, ribs and cranial bones continue to produce RBC throughout life.

The red blood cell is derived from a primitive precursor, a nucleated cell called **erythrocytoblast**, present within the bone marrow. It has no hemoglobin. It is converted to hemocytoblast, a generalized stem cell from which all blood cells form including erythrocytes and leucocytes. Development takes place in two main stages:

1. Maturation of the Cell

Hemocytoblast is converted to proerythroblast. The cell reduces in size and extrudes its nucleus. These changes require vitamin B_{12} and folic acid, which is normally obtained from the diet. Excess of it is stored in the liver. B_{12} absorption is dependent on the glycoprotein, an intrinsic factor, secreted by the parietal cells in the gastric glands. An intrinsic factor, vitamin B_{12} complex, is formed and its absorption takes place only when it comes to the ileum. Deficiency of B_{12} or folic acid affects red-cell production and leads to anemia.

Ribosome production is increased in the cell and mitotic division takes place leading to the formation of many small cells. Slowly, the cells start **hemoglobin synthesis** until they become bright red. This color is due to the formation of oxyhemoglobin. Hemoglobin is a complex protein containing globin and an iron-containing substance called **hem**. It is synthesized in the ribosomes. Hemoglobin increases and occupies a lot of space in the cell and pushes the other organelles which ultimately degenerate. The cell decreases in size and is now called a **normoblast**. Finally, hemoglobin occupies most of the cell and the nucleus and organelles are extruded. The cell formed is dumb-bell shaped and called a **reticulocyte**.

Reticulocytes escape the bone marrow and squeeze into the blood capillaries. The reticulocytes can be distinguished from the RBCs because they still contain some speckles of their nucleus. Within a few days, the reticulocyte completely loses all its nuclear material and becomes a full-fledged RBC.

The life span of an RBC is 120 days. The membranes of old RBCs become very fragile and the cells may rupture during passage through capillaries. These old and damaged RBCs are destroyed in the spleen and the iron from the hemoglobin is recycled to form new RBCs.

2. Regulation of Erythropoiesis

The production of red blood cells is equal to its destruction keeping the number sufficient to sustain adequate tissue oxygen levels.

Erythropoietin is produced in the kidney and liver in response to low oxygen levels.

Erythropoietin is bound to circulating red blood cells and when the cells decrease, it leads to a high level of unbound erythropoietin, which stimulates production in the bone marrow.

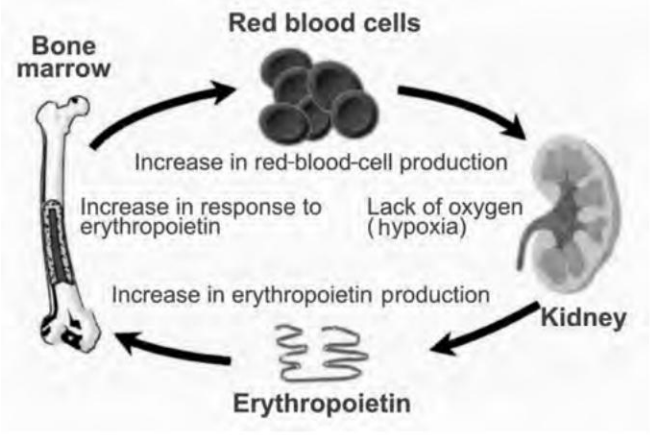


Fig. 15.3 *Erythropoiesis*

Thus, there is a feedback loop involving erythropoietin which helps regulate the process of erythropoiesis. When there is hypoxia, it stimulates more release of erythropoietin. This increases production of proerythroblasts and a larger number of reticulocytes is released. The oxygen-carrying capacity of blood is increased and hypoxia is reversed. Erythropoietin level decreases and red-cell formation stops. Hence, erythropoietin production is more at high altitudes, when there is hemorrhage or lung infection or after vigorous exercise.

The presence of erythropoietin is the main factor for red-cell formation to take place. Hence, even if there is hypoxia, and erythropoietin level is low, red-cell formation is not stimulated.

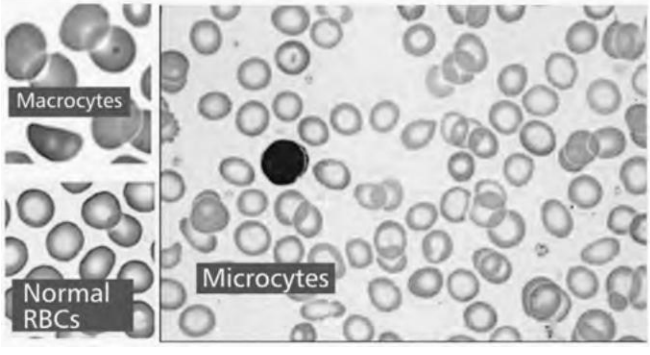


Fig. 15.4 *Normal and abnormal shapes of RBCs*

Red cells are finally hemolysed in the spleen, liver and bone marrow.

Sometimes v**ariation** is seen in the **structure** of erythrocytes.

Dots of basophilic materials appear in the red blood cells giving them a striped appearance. This is seen in lead poisoning and is called **punctate basophilism**.

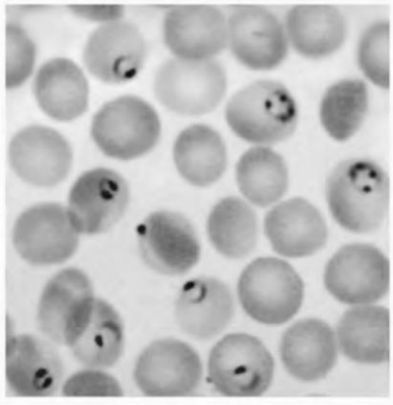


Fig. 15.5 *Parasitised red blood cells: P. Falciparum trophozoites*

Rings or twisted strands of basophilic material appear in the periphery of the red blood cells. This is also called the **goblet ring**, seen in certain types of anemia, viz., that occurring in malaria.

Some nuclear fragments are present in the ectoplasm of the red blood cells. These nuclear fragments are called Howell–Jolly bodies found in cases of B_{12} deficiency anemia.

15.4.2 Fate of Red Blood Cells

RBCs are terminally differentiated; that is, they can never divide. Young red blood cells can pass through the capillaries easily. As the cells become older, the cell membranes become more fragile and so are destroyed while squeezing through the capillaries. They live for about 120 days and then are ingested by phagocytic cells of the reticulo-endothelial system in the liver and spleen.

Most of the iron in the hemoglobin is reclaimed for reuse. The protein portion of the molecule is degraded into bile pigments and excreted by the liver. **Biliverdin** is first formed, which is completely reduced to **bilirubin**. This is bound to globulin and transported to the liver. It is excreted in bile. They are converted to urobilinogen and stercobilinogen and excreted in the feces.

15.4.3 Properties of Red Blood Cells

(a) Rouleaux Formation Rouleaux are stacks of red blood cells which form because of the discoid shape of the cells. The flat surface of the discoid RBCs give them a large

surface area to make contact and stick to each other; thus, forming a rouleaux.

When red blood cells are taken out from the body and allowed to remain stagnant for a certain period of time, they pile up one above another like a pile of coins. This property of the red blood cells is called rouleaux formation.

(b) Specific Gravity The specific gravity of red blood cells is 1.092 to 1.101.

(c) Suspension Stability During circulation, the red blood cells remain suspended uniformly in the blood as long as it is flowing. This property is called suspension stability.

(d) Packed Cell Volume (Hematocrit) The hematocrit, or Packed Cell Volume (PCV), is the proportion of blood volume that is occupied by red blood cells. It is normally about 46% in men and 38% in women.

When blood is taken out and centrifuged in a centrifuge tube for 30 minutes at a speed of 3000 rpm, the red blood cells settle at the bottom. Plasma remains above.

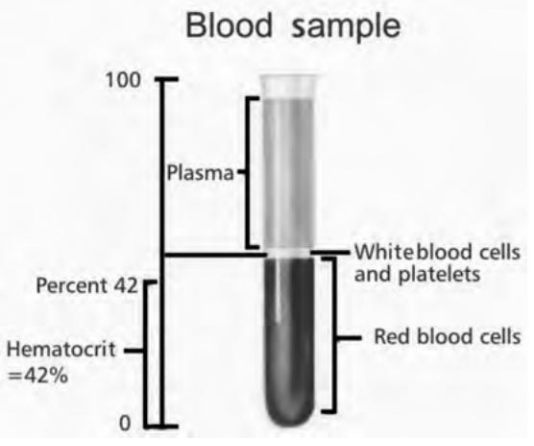


Fig. 15.6 *Packed cell volume*

Volume of plasma is 55%.

Volume of red blood cells is 45%.

This test is almost always done as part of a complete blood count. The hematocrit is expressed as a percentage.

Normal results vary, but, in general, are as follows:

Male : 40.7–50.3%

Female: 36.1–44.3%

Low hematocrit may be due to anemia, leukemia, bone-marrow failure, destruction of red blood cells, blood loss, rheumatoid arthritis and malnutrition.

High hematocrit may be due to dehydration as seen in burns and diarrhea, erythrocytosis, polycythemia vera, in people living at high altitudes and in chronic smokers.

(e) Hemolysis If RBCs are taken out of the body and kept in a hypertonic solution, they swell and then rupture, liberating hemoglobin. This property is called hemolysis.

(f) Erythrocyte Sedimentation Rate (ESR) ESR is the rate at which red blood cells settle down at the bottom of a container in a period of 1 hour. Details are discussed later.

(g) Agglutination Red blood cells contain a substance called antigens containing agglutinogens. When exposed to specific agglutinins, there is an antigen–antibody reaction leading to clumping of RBCs. This is agglutination.

15.4.4 Functions of Red Blood Cells

(a) Transport of Gases Erythrocytes transport oxygen from the lungs to the tissues. The hemoglobin in red blood cells combines with oxygen. 97% of oxygen is transported as oxyhemoglobin. They also transport carbon dioxide from the tissues to the lungs. The hemoglobin in the red blood cell combines with carbon dioxide to form carboxyhemoglobin. 30% of carbon dioxide is transported in this form.

Its shape increases the cell's surface area and facilitates diffusion of O_2 and CO_2 into and out of the cell. The lack of nuclei and organelles also contribute to increased hemoglobin content and gas-carrying capacity.

(b) Buffer Action Hemoglobin in red blood cell functions as a good buffer. It takes part in the maintenance of acid–base balance by regulating the hydrogen-ion concentration.

(c) Blood Group Determination Red blood cells carry the blood group antigens like A agglutinogen, B agglutinogen and Rh factor. This helps in determination of blood group.

(d) Maintenance of Viscosity RBCs help maintain the viscosity of blood.

15.4.5 Erythrocyte Sedimentation Rate (ESR)

Erythrocyte sedimentation rate is the rate at which red blood cells settle down at the bottom of a container in a period of 1 hour. This is found out by a common hematology test which is a nonspecific measure of inflammation. To perform the test, the blood with a suitable anticoagulant is permitted to stand in a tube, known as a Westergren's tube and the rate at which the red blood cells settle at the bottom in their own plasma is measured and reported in mm/h. This rate is known as erythrocyte sedimentation rate.

Since the introduction of automated analyzers into the clinical laboratory, the ESR test has been automatically performed.

1. Determination of ESR

There are two methods:

(a) Westergren's method

(b) Wintrobe's method

(a) Westergren's Method Here, a Westergren's tube is used which is 300 mm long and open at both ends. 1.6 mL of blood is diluted with 0.4 mL of 3.8% sodium citrate. The diluted blood is loaded in the Westergren's tube and the tube is fitted to the stand vertically. Reading is taken at the end of one hour.

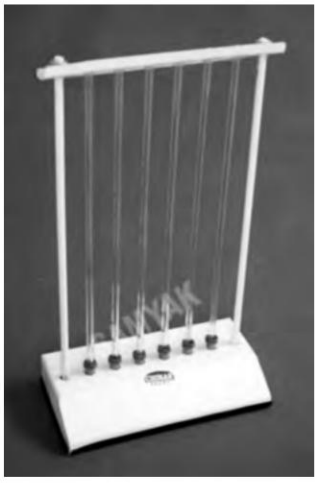


Fig. 15.7 *Apparatus for Westergren's method*

(b) Wintrobe's Method Here, a Wintrobe's tube is used which is short and open at one end. 1 mL of blood is mixed with an anticoagulant, EDTA. Blood is loaded in the tube up to the 'O' mark and the tube is placed on the Wintrobe's stand. At the end of one hour, ESR is read as the length of the plasma column above the cells.

2. Normal Values

In males : 3 to 7 mm in one hour
In females : 5 to 9 mm in one hour

ESR determination is a nonspecific screening test. It is of limited use as a screening test in symptomatic patients. A rapid sedimentation rate indicates tissue destruction which may be inflammatory or degenerative in origin. This test has prognostic value rather than diagnostic importance. The course of a disease can be predicted by this test, and it is possible to estimate the recovery.

ESR is increased in some chronic infective conditions like tuberculosis, collagen diseases like rheumatic fever and rheumatoid arthritis, and infective endocarditis.

ESR is decreased in allergic conditions, sickle-cell anemia and in polycythemia.

15.4.6 Hemoglobin

Hemoglobin is the colored pigment inside red blood cells that carries oxygen round the body. It is a chromo protein. It consists of two basic parts, the iron-containing pigment hem and the protein globin. Each red cell has 640 million molecules of hemoglobin.

The most common blood disorder is anemia in which inadequate hemoglobin causes weakness, pallor and sometimes, breathlessness. Further details are discussed in the section on anemia.

1. Normal Values

Adult males – 14–18 (16+2) g/dL of blood
Adult females – 12–16 (14+2) g/dL of blood
In newborns – 16–22 g/dL of blood; by 2 months it decreases to 9–14 g/dL
By 10 yrs – 12–14 g/dL

There may be slight decrease in hemoglobin level after 50 years of age.

Hemoglobin levels are the lowest in the morning and highest in the evening. It rises temporarily during excitement and exercise.

2. Synthesis of Hemoglobin

Hemoglobin is synthesized in the RBCs, in the bone marrow, in a series of steps in the mitochondria and cytosol of the immature red blood cells. Production continues throughout the development of RBC from the proerythroblast stage up to the reticulocyte stage. At this point, the nucleus is lost. Synthesis still goes on in the reticulocyte, till it loses its RNA after entering the blood.

Chemically, hem is conjugated to globin. Hem consists of 4 pyrrole groups linked to a nonferrous group and joined to each other by methane groups. Globin helps hem to keep iron in the ferrous state.

Certain substances help hemoglobin formation. Proteins containing histidine, phenylalanine and leucine, stimulate its formation. The main metal is iron. Others are cobalt, manganese and copper. Certain vitamins like B_{12}, folic acid, riboflavin and nicotinic acid are also useful for synthesis. Porphyrin III is also helpful in the synthesis of hemoglobin. The thyroxine hormone also plays a part in its synthesis.

3. Properties of Hemoglobin

The hemoglobin molecule combines loosely and reversibly with oxygen forming oxyhemoglobin, and then releases it readily in the tissue capillaries, where the gaseous tension of oxygen is much lower than in the lungs.

Oxygen binds loosely with the coordination bonds of an iron atom so that the combination is easily reversible. Also, the oxygen does not become ionic oxygen, but is carried as molecular oxygen to the tissues, where it is released into the tissue fluids still in the form of molecular oxygen and not ionic oxygen.

Hemoglobin also carries CO_2 as carbaminohemoglobin.

Hemoglobin can also combine with carbon monoxide to form carboxyhemoglobin, which is a firm combination; here

hemoglobin cannot combine with oxygen and asphyxia can occur.

It gives the red color to the red blood cells.

It can be easily crystallized and the crystals are specific for each animal species.

It carries more than 20 times its volume of oxygen.

Alterations in its structure can cause life-threatening diseases like sickle-cell anemia.

4. Functions

1. The most important function of hemoglobin is transport of oxygen to the tissues and transporting carbon dioxide to the lungs.
2. Hemoglobin is also a powerful buffering agent in the maintenance of blood pH levels.
3. It maintains the ionic balance.
4. During its metabolism, it forms pigments like biliverdin and bilirubin.

5. Estimation of Hemoglobin

Various methods, direct as well as indirect, can be used to estimate hemoglobin. The direct method includes the Tallquist method and Gower's method. The indirect methods are Haldane's carboxyhemoglobin method, Cyanhematin method, Wu's alkaline hematin method and Sahli's acid hematin method.

Fig. 15.8 *Apparatus for Sahli's acid hematin method*

In the **direct method,** a drop of blood is taken. The color of that drop of blood is directly compared against a printed color scale representing various concentrations of hemoglobin expressed in percentage.

In the **indirect method,** a sample of blood is taken and is treated with a particular chemical (depending upon the method).

This chemical, then reacts with hemoglobin and forms a compound of hemoglobin.

The color of that compound is matched with standard color plates.

15.5 WHITE BLOOD CELLS (LEUCOCYTES)

White Blood Cells (WBCs) are cells of the immune system, defending the body against both infectious disease and foreign substances. Five different types of leukocytes exist, but they are all produced and derived from a single cell in the bone marrow known as a hematopoietic stem cell. Leukocytes are found both in the blood and the lymphatic system. They are colorless, contain nuclei and some have granules in their cytoplasm.

After formation, they are transported to the different parts of the body, where they are used, specifically to areas of infection and inflammation, so as to provide a rapid and potent defense against any infection or any infectious agent present. Thus, the number of leukocytes in the blood is an indicator of disease.

The number of leukocytes and their properties such as volume, conductivity, and granularity, may change quantitatively and qualitatively due to activation following infection, the presence of immature cells, or the presence of malignant leukocytes in leukemia.

The life of granulocytes is short. Once released from the bone marrow, they normally stay 4 to 8 hours circulating in the blood and another 4 to 5 days in the tissues. When they die, they are destroyed by surrounding white blood cells and are replaced with new ones.

When there is serious infection, their total life span is further shortened to only a few hours as the granulocytes go rapidly to the infected area, perform their functions and in the process get destroyed themselves.

There are two main types of leucocytes.

- **Granular WBCs,** which have granules in their cytoplasm and the nuclei are multi-lobed. They are neutrophils, eosinophils and basophils.
- **Agranular WBCs,** which do not have granules in their cytoplasm and the nuclei are not lobed. They are monocytes and lymphocytes,

15.5.1 Formation or Synthesis

1. Granulocytes

Granulopoiesis occurs from the same type of stem cells called **myeloblasts** and takes place in the red bone marrow. Granulocytes follow a common line of development from myeloblast to myelocyte and then differentiate into three types.

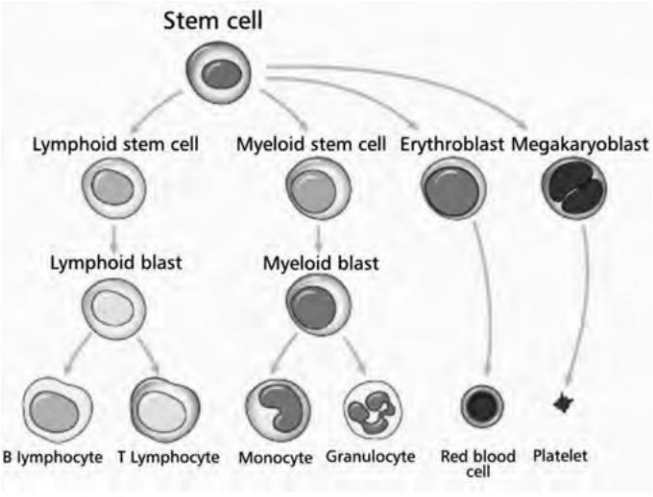


Fig. 15.9 *Steps of blood-cell formation (Refer colour figure)*

Myeloblasts are nongranular. Granules appear in the next stage and the cells are called myelocytes. The nucleus gets condensed in the third phase and lobulated in the last phase during circulation. There is loss of RNA and other cytoplasmic organelles while maturing.

Development takes 14 to 15 days, but this time is reduced when there is increased demand, as for example, in acute bacterial infection. The red marrow also contains a large reserve pool of mature granulocytes so that for every circulating cell there may be 50–100 cells in the marrow.

Mature cells pass actively through the endothelial lining of the marrow sinusoid into the circulation. Half the granulocytes adhere closely to the internal surface of the blood vessels and are called **marginating** cells. The other half circulate in the blood.

2. Lymphocytes

Lymphocytes are produced in the bone marrow from the lymphoblasts and prolymphocytes. Immature cells migrate to the thymus and other lymphoid tissues, including those found in bone marrow, and undergo further division, processing and maturation.

3. Monocytes

Monocytes are produced in the bone marrow, developing from nucleated precursors, the monoblasts and promonocytes. Mature cells remain in the blood for approximately 3–8 hours.

Monocytes are actively phagocytic and, on migration into the tissues, they mature into larger cells called **macrophages**, which can survive in the tissues for long periods. These cells form the mononuclear phagocytic cells of the reticuloendothelial system in the bone marrow, liver, spleen and lymph nodes.

15.5.2 Morphology

1. Neutrophils

Neutrophils or polymorphonuclear (PMN) leukocytes have a multilobed nucleus, which may appear like multiple nuclei, hence the name polymorphonuclear leukocyte. The diameter of the cell is 10 to 12 microns. 65–70% of WBCs are neutrophils. Neutrophils are ameboid in character.

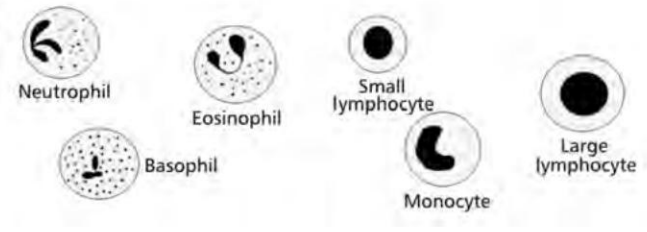


Fig. 15.10 *Types of white blood cells*

The cytoplasm has fine granules that are faintly pink and the granules become violet on staining with acidic and basic stains.

2. Eosinophils

Eosinophils have coarse and larger granules which stain bright red or orange with eosin. The nucleus is bi-lobed. The diameter of the cell varies from 10 to 14 microns. Granules contain many substances like peroxidase, major basic protein and neurotoxin. They are neither markedly motile nor phagocytic like the neutrophils.

3. Basophils

Basophils are the least common of the granulocytes. They contain large cytoplasm granules. The granules stain purple blue with basic dyes like methylene blue. The nucleus is bi-lobed. Diameter of the cell is 8 to 10 microns.

4. Monocytes

Monocytes are the largest leucocytes. Their diameter is 14 to 18 microns. The nucleus is either in the center of the cell or is pushed to one side and is round, oval, horseshoe- or kidney-shaped.

In the tissues, monocytes mature into different types of macrophages at different anatomical locations.

5. Lymphocytes

Lymphocytes have less amount of cytoplasm because the nucleus which is oval or kidney-shaped occupies the whole of the cytoplasm.

Depending upon the size, the lymphocytes are of two types.

- Large lymphocytes are the younger cells and have a diameter of 10 to 12 microns.
- Small lymphocytes are the older cells and have a diameter of 7 to 10 microns.

Depending upon the function, there are two main types of lymphocytes; B cells and T cells.

Total WBC count is 4,000 to 11,000/cu mm of blood.

Differential WBC Count

Neutrophils	:	50 to 70%	–	3000 to 6000 / cu mm
Eosinophils	:	2 to 4%	–	150 to 450 / cu mm
Basophils	:	0 to 1%	–	0 to 100 / cu mm
Monocytes	:	2 to 6%	–	200 to 600 / cu mm
Lymphocytes	:	20 to 30%	–	1500 to 2700 / cu mm

15.5.3 Functions

Neutrophils defend against bacterial or fungal infection. They can squeeze through the pores of the blood vessels through diapedesis.

Many chemical substances are released by damaged cells in the infected area and neutrophils are attracted towards them. This is called **chemotaxis**. They could be bacterial or viral toxins, degenerative products of the inflamed tissue and several reaction products. The neutrophils are very active in phagocytosing bacteria and are present in large amount in the pus of wounds. These cells are not able to renew their lysosomes, used in digesting microbes, and die after having phagocytosed a few pathogens.

Eosinophils contain peroxidase, major basic protein and neurotoxin which become cytotoxic to the invading organisms.

They are active against helminths. They damage the parasites by causing distension and detach the sheaths of these organisms. They destroy the parasite by means of complete disintegration. Eosinophils are neurotoxic to some of the parasites. They destroy the nerve fibers of the parasites and paralyze them.

They are also the predominant inflammatory cells in allergic reactions and their count increases in asthma and hay fever.

Basophils play an important part in the allergic response as they have IgE on their surface, and when the IgE binds to the specific allergen, chemical mediators are released causing allergic symptoms.

Basophils play an important role in healing processes after inflammation and in acute hypersensitivity reactions. The number of basophils is increased during the healing process.

Certain important substances like histamine, heparin, proteases, myeloperoxidase and hyaluronic acid are released from their granules. These substances cause an acute hypersensitivity reaction by causing vascular changes and by increasing capillary permeability. They exaggerate the inflammatory responses and prevent intravascular blood clotting. Histamine is the major factor in the allergic response associated with inflammation.

Monocytes are responsible for phagocytosis of foreign substances in the body using proteins such as antibodies or complements that coat the pathogen, as well as by binding to the microbe directly. They are also capable of killing infected host cells via an antibody.

They can squeeze through the pores of the blood vessels by diapedesis and migrate from the bloodstream to other tissues and then differentiate into macrophages or dendritic cells. Macrophages are responsible for protecting tissues from foreign substances.

The **B cell lymphocytes** make antibodies that attack bacteria and toxins while the **T cells** attack body cells themselves, when they have been taken over by viruses or have become cancerous. Lymphocytes secrete products called lymphokines that modulate the functional activities of many other types of cells and are often present at sites of chronic inflammation. Thus, they play an important role in immunity and defending the body against disease.

15.5.4 Variations

- Physiological
- Pathological

1. Physiological Variations

- In infants, the WBC count is 20,000/cu mm and in children it is 10,000 to 15,000/cu mm of blood.
- The WBC count is slightly more in males. In females, it is increased during menstruation, pregnancy and childbirth.
- The cell count is minimal early in the morning and maximum in the afternoon.
- The count increases slightly during exercise.
- The count decreases during sleep.
- The count increases during emotional stress.

2. Pathological Variations or Disorders

Discussed later

15.6 PLATELETS (THROMBOCYTES)

Platelets are small, colorless, irregularly shaped anuclear cells, 2–4 μm in diameter, which are derived from fragmentation of megakaryocytes. Thus, they are actually not true cells but merely circulating fragments of cells. They are spherical or rod-shaped but, sometimes, they are of dumb-bell, comma,

cigar or any other unusual shape. The average life span of a platelet is between 8 and 12 days.

The platelet count is normally 2 to 4 lacs/ cu mm of blood. The count can vary slightly according to menstrual-cycle phase, decrease during near-term pregnancy (gestational thrombocytopenia), and increase in response to inflammatory cytokines (secondary, or reactive, thrombocytosis). Platelets are eventually destroyed, primarily, by the spleen.

15.6.1 Formation

Platelets are produced in the bone marrow through thrombopoiesis. They are formed in the cytoplasm of a very large cell, the megakaryocyte, also called the **giant cell**. The cytoplasm of the megakaryocyte fragments at the edge of the cell, called **platelet budding**, and forms megakaryoblast. They mature in about 10 days.

There is probably a feedback mechanism as the platelet count remains fairly constant in health, and platelet production is reduced following an infusion of platelets and increased following a removal of platelets. This has, however, not been proved.

15.6.2 Structure

Platelets are composed of membrane structures, microtubules, cytoskeleton, contractile proteins and granules. The cell membrane is 6 nm thick and is coated with glycoprotein which prevents adherence of platelets to normal endothelium but causes adherence to injured areas, e.g., damaged endothelium. Microtubules and granules are found in the cytoplasm. There are also proteins, enzymes and hormones.

Microtubules are tubelike structures forming a ring around the cytoplasm below the cell membrane.

The cytoskeleton provides a framework to anchor the platelet membrane. There are three kinds of granules in platelets, which are intrinsic to the platelet.

The contractile proteins are actin and myosin and thrombosthenin, which can cause the platelets to contract and is responsible for clot retraction. There is also a growth factor and an intrinsic factor.

Enzymes present are Adenosine Triphosphatase (ATP) and the enzymes necessary for synthesis of prostaglandins.

The hormones are adrenaline, serotonin and histamine.

The canalicular system provides a direct connection between the interior and the surface of the platelet for plasma ingredients to enter into the platelet as well as for exit of its own ingredients.

15.6.3 Functions

Platelets have the property of adhesiveness, aggregation and agglutination.

Platelets aggregate, or clump together, using fibrinogen as a connecting agent. Activated platelets will adhere to the collagen that is exposed by endothelial damage.

Aggregation and adhesion act together to form the platelet plug. Myosin and actin filaments in platelets are stimulated to contract during aggregation, further reinforcing the plug and are responsible for clot retraction.

The platelet-derived growth factor helps to repair the endothelium of the ruptured blood vessel.

Platelets engulf foreign bodies and kill them by phagocytosis.

Their sticky surface lets them, along with other substances, form clots to stop bleeding.

15.6.4 Variations

1. Physiological Variations

Platelets are less in infants and reach normal values at the third month. It is reduced in females during menstruation. The count increases during meals and at high altitudes.

2. Pathological Variations

Discussed later.

15.7 COAGULATION OF BLOOD

Coagulation is a complex process by which blood forms clots. It is an important part of hemostasis. A damaged blood-vessel wall is covered by platelets, a fibrin-containing clot is formed to stop bleeding and beginning of repair of the damaged vessel starts. Disorders of coagulation can lead to an increased risk of bleeding (hemorrhage) or clotting (thrombosis). Coagulation involves both a cellular (platelet) component and a protein (coagulation factor) component.

The factors involved in the process are

Factor I	Fibrinogen
Factor II	Prothrombin
Factor III	Thromboplastin
Factor IV	Calcium
Factor V	Labile factor, proaccelerin
Factor VI	Not known
Factor VII	Stable factor, proconvertin
Factor VIII	Antihemophilic factor A, antihemophilic globulin
Factor IX	Christmas factor, antihemophilic factor B
Factor X	Stuart–Prower factor
Factor XI	Plasma thromboplastin antecedent, antihemophilic factor C
Factor XII	Hageman factor
Factor XIII	Fibrin-stabilizing factor

These numbers represent the order in which they were discovered.

Coagulation begins as soon as there is damage to the endothelium of the blood vessel. Platelets immediately adhere to macromolecules in the subendothelial tissues and then aggregate to form a plug at the site of injury; this is called **primary hemostasis**. **Secondary hemostasis** occurs simultaneously. Platelets stimulate local activation of plasma coagulation factors. The prothrombin activator acts on the plasma protein prothrombin and converts it to thrombin which acts on fibrinogen and converts it to fibrin. There is generation of a fibrin clot which traps the blood cells. It reinforces the platelet aggregate which strengthen the platelet plug. Later, the platelets aggregate and the fibrin clot is broken down. The clot shrinks, serum is squeezed out and wound healing occurs.

Fibrinolysis is the breaking down of the clot. Plasminogen which is present in the clot is converted to plasmin by the activators released from the damaged cells. Fibrin is broken down by plasma to soluble products which are removed by the phagocytes. Thus, the clot is removed and the blood-vessel wall becomes normal.

The process of coagulation works on positive feedback mechanism and is controlled by mechanisms which are self-limiting. Thrombin binds to the thrombin receptor on the cells, lining the blood vessels and hence is in inactive form. Natural anticoagulants like heparin are present in the blood which inactivate clotting factors.

The coagulation system overlaps the immune system. Microbes are physically trapped in the blood clots and some products of the coagulation system can contribute to the immune system by their ability to increase vascular permeability.

Thus, coagulation plays a very important role in maintaining homeostasis in the body.

15.8 BLOOD GROUPS

A blood type, or blood group, is a classification of blood based on the presence or absence of inherited antigenic substances on the surface of Red-Blood-Cells (RBCs). These antigens may be proteins, carbohydrates, glycoproteins or glycolipids, depending on the blood-group system. Several of these red-blood-cell surface antigens that stem from one allele (or very closely linked genes), collectively form a blood-group system.

Karl Landsteiner's work made it possible to determine blood groups. Blood types are inherited and represent contribution from both parents. A total of 30 human blood-group systems are now recognized by the International Society of Blood Transfusion (ISBT). Of these, the ABO and Rh systems are the most important ones.

15.8.1 ABO Blood-Grouping System

The ABO blood group system is the most important blood-group system in human blood transfusion. The antigens (agglutinogen) are located on the surface of the red blood cells and the antibodies (agglutinins) are in the blood plasma. There are two antigens and two antibodies that are mostly responsible for the ABO types. The specific combination of these four components determines an individual's type in most cases. The ABO antigens are developed well before birth and remain throughout life. The associated anti-A antibodies and anti-B antibodies are usually immunoglobulin M (IgM) antibodies. ABO IgM antibodies are produced in the first years of life by sensitization to environmental substances like viruses, bacteria and food.

Accordingly, there are four different kinds of blood groups: A, B, AB or O. (See Table 15.2)

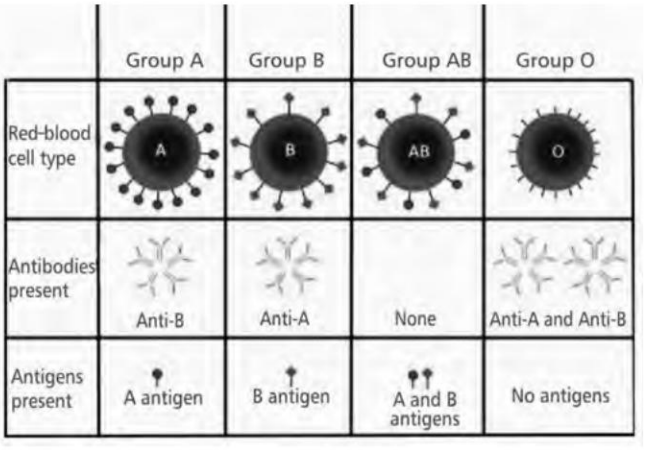


Fig. 15.11 *Types of blood groups*

Table 15.2 *Types of blood groups*

Blood group	*Antigens—agglutinogen*	*Antibodies—agglutinins*	*Recipient*	*Donor*
Group A	A antigens	Anti-B	From A or O individuals	Individuals of A or B
Group B	B antigens	Anti-A	From B or O individuals	Individuals of group A or B
Group AB	A and B antigens	None	From any group	
			Universal recipient	AB individual
Group O	No antigens	Anti-A and Anti-B	From group O	From all groups Universal donor

15.8.2 Rh (Rhesus) Factor Blood-Grouping System

The Rh blood-group system is the most important blood-group system after ABO. It consists of 50 blood-group antigens on the red blood cell's surface of which 6 are the most important—D, d, C, c, E and e. Those having the antigen are called Rh positive Rh+ve (85%). Those who do not have the factor are called Rh negative Rh–ve (15%) and it refers to D antigen.

Rh+ve individuals can receive blood from Rh-ve persons without any complication. But, if a person with Rh-ve blood receives blood from a person with Rh+ve blood, he can develop Rh antibodies in the blood plasma.

15.8.3 Determination of Blood Groups

According to Landsteiner's law, if an agglutinogen is present in the red blood cell of a person, the corresponding agglutinin must be absent in the plasma. While if an agglutinogen is absent in the person, the corresponding agglutinin must be present in the plasma.

A sample of blood is mixed with different samples of plasma known to contain different antibodies. For example, if plasma which contains anti-A antibodies makes the red cells in the blood clump together then A antigens are present on the blood cells. Or, if plasma which contains rhesus antibodies makes the red cells in the blood clump together then rhesus antigens are present on the blood cells. By doing a series of such tests it is possible to determine what antigens are on the red blood cells and thus the blood group can be determined.

Routine blood grouping checks for ABO and rhesus status.

1. Universal Donor

Group O people have neither A nor B antigens in their cell membranes. They can safely give blood to A, B, AB or O types. They are called universal donors.

2. Universal Recipient

AB group people do not have anti-A or anti-B antibodies. They can have A, B or O blood transfusion without any complication, as there are no antibodies to react with them. They are called universal recipients.

15.9 BLOOD TRANSFUSION

Blood transfusion is the process of transferring blood or blood-based products from one person to another.

15.9.1 Indications

1. Acute hemorrhage—external or internal
2. Massive blood loss due to trauma
3. Before surgery, if there is severe malnutrition and hypoproteinemia; and during surgery to replace blood lost during the procedure or after surgery, if there is infection or septicemia
4. Deep burns
5. For treatment of anemia when hemoglobin level is very low
6. In coagulation disorders—hemophilia, thrombocytopenic purpura
7. In sickle-cell disease, frequent transfusions may be required
8. During chemotherapy when RBC level falls
9. Whole blood transfusion given in Hodgkin's disease, leukemia and aplastic anemia

15.9.2 Types of Blood Transfusion

1. **Whole blood transfusion** is of five types:
   - The stored blood from blood bank
   - Warm blood used during cardiopulmonary operations to prevent cardiac arrest
   - Filtered blood, filtered through a membrane to filter leucocytes and platelet aggregates
   - Auto transfusion, where the patient's own blood is transfused, especially in ruptured spleen or liver; blood is collected, filtered and transfused
   - Exchange transfusion done in erythroblastosis fetalis (in newborn infants), in myasthenia gravis and in Guillian–Barré syndrome
2. **Packed red cells** are given in chronic anemia, elderly patients, and persons with low cardiac reserve and in children
3. **Platelet-rich plasma**

15.9.3 Complications of Blood Transfusion

- Transfusion reactions
- Transmission of diseases

1. Transfusion Reactions

- **Incompatibility** occurs due to incompatible blood, or hemolysed blood or transfusion of blood after the expiry date.
- **Pyrexia reactions** occur due to improperly sterilized transfusion sets, presence of pyrogens or infection in the donor blood.
- **Allergic reactions** develop within a few hours of transfusion and sometimes, some cases may develop anaphylactic shock.

2. Transmission of Disease

Certain diseases are transmitted if the donor's blood is not tested properly before transfusion. They are serum hepatitis, HIV virus, bacterial infections and malaria.

Besides these reactions, certain miscellaneous reactions can take place like acid–base imbalance, hypothermia, hyperkalemia, citrate toxicity and failure of coagulation.

15.10 DISORDERS OF RBC

1. Anemia

Anemia is defined as a state in which the blood hemoglobin level is below the normal range for the patient's age, sex, and altitude of residence. Sufficient oxygen is not supplied to the tissues. The rate of production of mature cells, which enter the blood, is not enough to compensate for the loss or hemolysis.

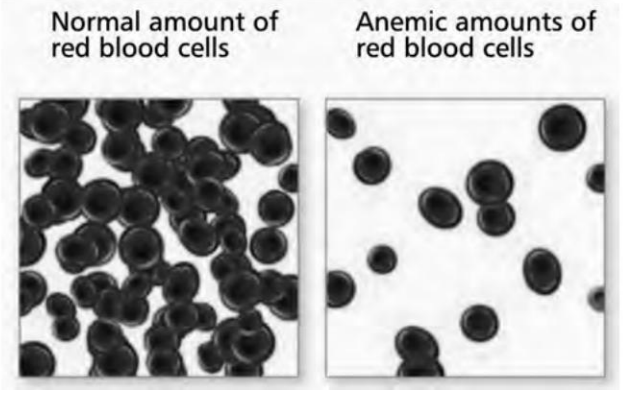


Fig. 15.12 *Amount of red blood cells shown in a peripheral smear*

Classification

Classification depends on the cause.

(i) Anemia due to Deficiency of Factors Essential for Normal Blood Formation

- Deficiency of iron
- Vitamin B12 and Folic acid deficiency and/or proteins

(ii) Anemia due to Excessive Blood Destruction

Here, red cells are destroyed while in circulation or removed prematurely, as in overactive spleen, or because the cells are abnormal. Chronic malaria produces anemia by RBC destruction.

(iii) Anemia due to Hypoplasia or Aplasia of the bone marrow due to toxins, irradiation, cancer, drugs, etc.

(iv) Hereditary Anemias

- Sickle-cell anemia
- Thalassemia

2. Iron-deficiency Anemia

Iron-deficiency anemia is by far the commonest cause of anemia.

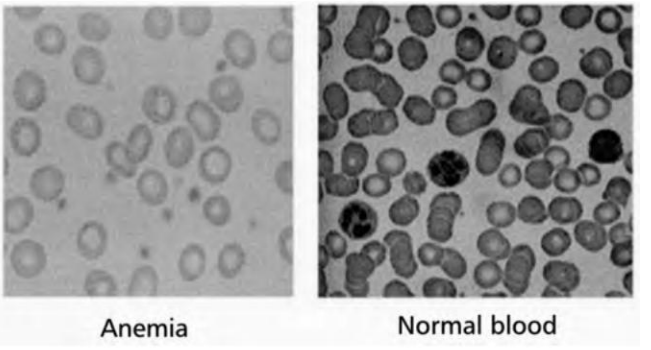


Fig. 15.13 *Iron-deficiency anemia*

The normal daily requirement of iron in males is 2 mg and in females, is 3 mg.

Persons with anemia have **symptoms** like weakness, tiredness, dizziness, light-headedness, and gastrointestinal disturbances. With worsening, symptoms like breathlessness, palpitation and paresthesias develop. In severe cases there is edema, tachycardia, cardiac dilatation and signs of cardiac failure.

Pathophysiology It could be physiological like postnatal growth spurt, adolescent growth spurt, delayed weaning of babies who are not given enough mixed diet, menstruation or pregnancy.

It can occur due to inadequate intake or deficiency in the diet, due to more requirement or poor absorption, e.g., malabsorption syndrome. This leads to deficiency of iron in the bone marrow.

It can also occur due to excessive blood loss like bleeding from gums or GI tract like bleeding peptic ulcer, ulcerative colitis, etc.

It can occur due to abnormalities of absorption from the stomach, duodenum or jejunum as seen in malignancy or resection of a part of the stomach.

It can also occur due to repeated blood donations at rather short intervals.

Pica is a craving for coal, earth, mud, chalk, etc., and is a common cause for iron-deficiency anemia, especially in children.

Investigations have to be done to confirm iron-deficiency anemia and to determine the cause of iron deficiency.

Routine investigations for confirming anemia are **blood examination** which shows reduced hemoglobin and reduced red-cell count.

Peripheral smear examination shows microcytosis, hypochromia, elliptical cells and poikilocytes.

Other indices which help diagnose anemia are the following:

- **Mean corpuscular diameter** which is 7.2 u.
- **Mean cell volume** is the average volume of cells measured in femtoliters (fl = 10^{-15} litre).
- **Mean Corpuscular Hemoglobin** (MCH) is the measure of hemoglobin in one RBC and the normal range is 27–32. It is decreased in hypochromic anemia and increased in hyperchromic anemia.
- **Mean Corpuscular Hemoglobin Content** (MCHC) is the measure of hemoglobin per 100 mL of blood. The normal range is 30–35, which is decreased in hypochromic anemia and increased in hyperchromic anemia.

The cause of the deficiency must be found out before treatment and investigations like stool examination, gastrointestinal endoscopy and barium studies should be carried out.

Treatment is directed towards correcting the iron deficiency and eradicating the underlying cause.

Diet should be rich in iron. Oral iron therapy is given and if necessary injectable iron and blood transfusion is carried out.

After 6 to 8 weeks, hemoglobin level begins to normalize.

Iron therapy should be continued for 2 to 3 months after correction of anemia.

If there is gross focal infection, it should be treated.

Abnormal blood loss should be controlled.

Parenteral iron therapy is for those very few patients who are genuinely unsuitable for oral therapy or due intolerance to oral iron or who do not take iron regularly or for patients with gastrointestinal disease.

An attempt should be made to find out the cause and treat it, e.g., piles, peptic ulcer, worm infestations.

3. Megaloblastic Anemia

Vitamin B_{12} and folic acid are essential for RNA and DNA synthesis and deficiency of one or both leads to reduction in the rate of RNA and DNA synthesis, leading to delayed cell division.

This type of anemia occurs due to folate deficiency, which can be because of deficient intake, increased demand as in pregnancy, malabsorption as in tropical sprue, and inadequate utilization as seen in liver disease.

Vitamin B_{12} deficiency also causes megaloblastic anemia and can be due to increased requirement as seen in pregnancy, infancy, achlorhydria (absence of acid in the stomach) induced malabsorption, deficient intake as in malnutrition, inadequate absorption due to deficient intrinsic factor (pernicious anemia), gastrectomy, biological competition for B_{12} as in diverticulosis and in infection by the parasite *D. latum*. Bacteria and parasites utilize B_{12} and render it unavailable to the host.

Clinical features are those of iron-deficiency anemia.

Bilateral symmetrical peripheral neuropathy (tingling and numbness in feet and hands) is the distinguishing feature, and there is difficulty in balancing while walking.

Mild splenic enlargement, mental changes, irritability, sleeplessness may also occur with folate deficiency.

Pathophysiology During normal erythropoiesis, with cell division the cells are smaller as the division is quick and cells do not have time to enlarge. With vitamin B_{12} and folic-acid deficiency, due to delay in cell division, cells can grow larger than normal. Maturation also does not take place and the majority of cells entering the circulation are megaloblasts.

Vitamin B_{12} requires an intrinsic factor in the stomach for its absorption. Hence, consequent to defective production of the intrinsic factor by the stomach, vitamin B_{12} deficiency occurs due to a failure in its assimilation. This is the cause of **Addisonian pernicious anemia**, which is the most important type of megaloblastic anemia. There may be an inborn deficiency of intrinsic-factor secretion causing juvenile pernicious anemia.

Certain investigations like peripheral smear examination are done, which shows macrocytic anemia—red blood cells are large, oval in shape with anisocytosis and poikilocytes. In severe cases, a few nucleated red cells or hemoglobinised megaloblasts are seen.

Hemoglobin estimation is often reduced, even low.

Serum B_{12} level is very low and often less than 50 ng/L.

So, also, is the low serum folate level.

Treatment is directed towards **specific therapy and supportive therapy.**

Vitamin B_{12} is given as cyanocobalamin or hydroxycobalamin and is given intramuscularly or intravenously).

The initial dose of hydroxycobalamin is 1000 mcg, given deep intramuscularly daily for one week.

The maintenance dose is 1000 mcg, deep intramuscularly once in 3 months.

Oral iron therapy should be started soon after the commencement of vitamin B_{12} therapy.

Folic acid is given at an initial dose of 5 mg orally, followed by a maintenance dose of 5 mg once a week.

Folic acid must never be given alone without vitamin B_{12} in B_{12} deficiency anemia because the neurological features of vitamin B_{12} deficiency may be aggravated or precipitated if folic acid is given alone.

Supportive therapy is by treating infections, blood transfusions, if indicated and treatment of cardiac failure.

Addisonian pernicious anemia is a megaloblastic macrocytic anemia resulting from a failure of secretion of the intrinsic factor by the stomach, other than from total gastrectomy. In the absence of an intrinsic factor, dietary vitamin B_{12} is not absorbed and this results in vitamin B_{12} deficiency.

4. Hemolytic Anemia

Hemolytic anemia results from an increased rate of red-cell destruction. The life span of red cells is shortened.

There are symptoms of anemia including mild jaundice and splenomegaly.

Pathophysiology It can occur due to intra-erythrocyte and extra-erythrocyte defects.

Intra-erythrocyte defects could be congenital like G6PD deficiency, sickle-cell anemia and thalassemia or acquired like auto-immune conditions.

Extra-erythrocyte defects are non-immune mechanisms like malaria, mechanical causes like burns and due to certain drugs, e.g., Dapsone.

Routine investigations like a complete blood examination is carried out, including a fragility test (time taken for breaking down of RBCs).

Heinz bodies in red cells indicate G6PD deficiency and unstable hemoglobin.

Positive Coomb's test is present in acquired hemolytic anemia.

IgG antibodies are detected in auto-immune hemolytic anemia.

Treatment of hemolytic anemia is supportive in the form of blood transfusions, treatment of infections and splenectomy in selected cases.

Specific therapy, if available, is given for individual diseases.

5. Aplastic Anemia

Aplastic anemia is a stem-cell disorder in which an acellular or markedly hypocellular bone marrow results in pancytopenia, i.e., anemia, granulocytopenia, thrombocytopenia.

Aplastic anemia is a rare disorder and may occur at any age but is usually seen in young adults.

Symptoms of aplastic anemia are that of pancytopenia, i.e., symptoms of anemia. Granulocytopenia leads to decreased immunity and various infections like oral ulcers and lung infection; and thrombocytopenia results in bleeding tendency like epistaxis, menorrhagia, petechiae, etc.

General features of anemia are present like pallor of the mucus membranes; petechiae, signs of infection, etc., but jaundice, splenomegaly and lymphadenopathy are absent.

The presence of these must prompt one to search for an associated disease or think of an alternate diagnosis.

Pathophysiology The condition is idiopathic but certain causes are known to cause this condition. Certain drugs like antibacterial drugs, antirheumatic drugs, antidiabetics and anticancer drugs can cause this anemia.

Viral infections like viral hepatitis, pancreatitis, radiation and certain chemicals like benzene and DDT can cause aplastic anemia.

A careful history into exposure to drugs, chemicals, radiation and viral infection should be taken.

Blood examination reveals reduced hemoglobin, marked anemia, reduction in absolute leukocyte count (especially neutropenia), ESR is raised, and platelet production is often most severely affected.

Bone-marrow study reveals a markedly hypocellular or acellular marrow.

Treatment first involves withdrawal of the causative agent. Infection and hemorrhage should be prevented and treated. Transfusion of packed cells and platelets may be necessary.

Transplantation of hemopoietic stem cells is tried.

Bone-marrow transplantation is the treatment of choice in persons below 40 years when an HLA matched donor is available.

6. Sickle-cell Anemia

Sickle-cell anemia is an autosomal recessive genetic blood disorder, where there are abnormal hemoglobin molecules which on deoxygenation are mis-shapen and lead the red blood cells to assume an abnormal, rigid, sickle shape. There is anemia. The patient becomes highly susceptible to bacterial infections. (See Fig. 15.14)

Pathophysiology Sickle-cell anemia usually presents itself in childhood. It is seen more in people living in tropical and subtropical regions. Blacks are more affected.

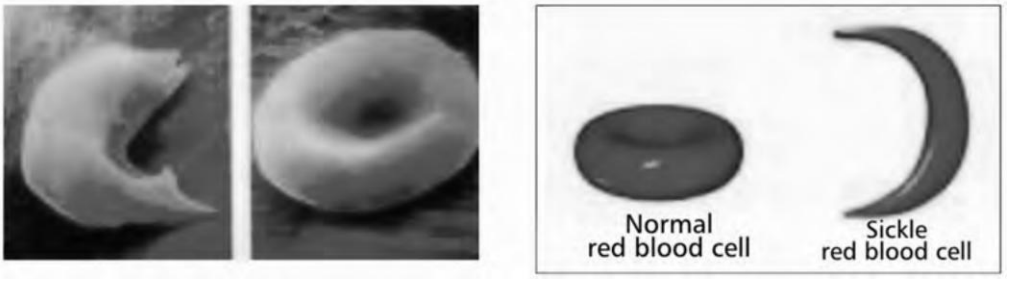


Fig. 15.14 *Sickle cell and normal cell*

It is an inherited, lifelong disease and these people inherit two copies of the sickle-cell gene—one from each parent.

These cells are stiff and sticky and don't easily move in the blood vessels. They form clumps and get stuck in the blood vessels. The clumps block the blood flow to the limbs and organs leading to pain, infection and organ damage.

The number of red blood cells is low because the sickle cells die in 10 to 20 days and the bone marrow cannot make new red blood cells fast enough to replace these dead cells.

7. Thalassemia

Thalassemia, also known as Mediterranean anemia (found commonly in people living in the Mediterranean), is a group of inherited disorders where there is reduced globin synthesis resulting in reduced hemoglobin production. The hemoglobin is fragile and breaks sooner than normal. Hence, there is lack of hemoglobin, resulting in anemia.

Pathophysiology Four genes are necessary for making enough alpha globin protein chains. If one or two of the four genes are missing, alpha thalassemia trait occurs. If more than two genes are missing, severe anemia occurs. Two genes, one from each parent, are needed for making beta globin protein chains. If one or both genes are altered, beta thalassemia occurs.

Defect in clot formation or overactive fibrinolytic systems can cause bleeding disorders. Hypercoagubility disorders can occur due to defects in the anticoagulation system or defective fibrinolytic systems.

15.11 DISORDERS OF WBC

1. Leucopenia

Decrease in total white cell count below 4000/cu mm is known as leucopenia and is seen in viral infections, typhoid fever, cirrhosis of liver, disorders of spleen, pernicious anemia, etc. Leucopenia occurs, after prolonged use of certain drugs like Amidopyrine and Phenacetin, and may even produce agranulocytosis.

2. Leucocytosis

Increase in total leucocyte count above 11000/cu mm is called leucocytosis. It is seen in acute infections, allergy, common cold, glandular fever, etc.

- **Neutrophilia** or neutrophilic leucocytosis is increase in the neutrophil count. It is seen in acute infections, after acute hemorrhage, metabolic disorders, poisoning by lead, mercury, etc.
- **Eosinophilia** is increase in eosinophil count. It is seen in allergic conditions, asthma, parasitic infestation, malaria, filariasis, scarlet fever.
- **Basophilia** is increase in basophil count. It is seen in small pox, chicken pox, polycythemia vera and worm infestations.

3. Monocytosis

This is increase in the number of monocytes. It is seen in long standing infections, protozoal infections, malnutrition and rickets.

4. Lymphocytosis

This is increase in lymphocyte count. It is seen in chronic infections like tuberculosis, in syphilis, auto-immune diseases like rheumatoid arthritis, in malaria, glandular fever and *kala azar*.

5. Leukemia

Leukemia is a malignancy of the blood or bone marrow and is characterized by an abnormal, uncontrolled proliferation of white blood cells and/or their precursors. The count could go up to 1,000,000/cu mm. As the bone marrow is filled with leukemic blast cells, there is associated, anemia, leucopenia and thrombocytopenia.

Pathophysiology In most of the cases, the cause is unknown. Several factors are associated with the development of leukemia.

They are exposure to ionizing radiation, certain chemicals and toxins.

Increase in myeloid leukemia was seen after atomic bombing in Japan. Increased incidence of leukemia is seen in children after use of radiographs during pregnancy. Also, in those where radiotherapy is used for ankylosing spondilitis. Radiation produces changes in the precursors of the leucocytes. DNA may be damaged and some of them may be destroyed but most of them proliferate at a very rapid rate.

Chemicals and cytotoxic agents also alter the DNA of the white cell precursors.

Some people have a genetic predisposition, such as those affected with Down's syndrome and Fanconi's anemia. There is a greatly increased incidence of leukemia in the identical twins of patients with leukemia.

One rare form of T-cell lymphoma appears to be associated with a retrovirus.

Immune deficiency states are associated with an increase in hematological malignancy.

Myelogenous leukemias involve the pluripotent myeloid stem cells.

Lymphocytic leukemias involve immature lymphocytes and their precursors. They arise in the bone marrow but, infiltrate the spleen, lymph nodes and central nervous system and less commonly other tissues.

Clinically and pathologically it is of two forms—acute and chronic.

They are further subdivided according to which kind of blood cell is affected:

- Lymphoblastic or lymphocytic leukemias
- Myeloid or myelogenous leukemias

(a) Acute Leukemia Acute leukemia is characterized by failure of cell maturation and rapid increase of immature blood cells. The bone marrow is filled with these cells and ultimately spills into the blood. Onset is sudden and progression is rapid. They are the most common forms of leukemia in children. Acute myeloblastic type is seen mostly between 25–60 years of age. Acute lymphoblastic type occurs commonly below 10 years of age.

Symptoms are in the form of fever, fatigue, frequent infections, bleeding tendency, weight loss and painless lumps in the armpit, groin, neck or mediastinum. Sometimes diagnosis is done on routine tests for some other condition.

Routine blood **investigations** are done like blood count and differential count.

The aim of **treatment** is to destroy leukemic cells without destroying residual normal stem-cell compartment. Drugs used are Vincristine, Prednisolone and Methotrexate. The only hope of cure is bone-marrow transplantation.

(b) Chronic Leukemia Chronic leukemia is distinguished by the excessive build up of relatively mature, but still abnormal, white blood cells. Chronic granulocytic leukemia mostly occurs between 22–40 years. There are increased immature granulocytes in the blood. In chronic lymphocytic leukemia, there is hyperplasia of lymphoid tissue throughout the body and high lymphocyte count. It occurs, most commonly, between the ages of 50–70 years.

Besides other causes, there is a chromosome abnormality known as Philadelphia (Ph) chromosome where there is a break in Chromosome 22.

Chronic leukemia may not have any early **symptoms.** 10–12% of patients are asymptomatic. Symptoms could be only pain under the ribs or night sweats. There may be lethargy, loss of weight, abdominal pain and 90% have splenomegaly.

Blood examination is the most useful **investigation** but, bone-marrow material must be examined for chromosome analysis to demonstrate the Philadelphia (Ph) chromosome.

Treatment in the form of chemotherapy is given. Busulphan, Hydroxyl urea and Alpha interferon are used. Bone-marrow replacement gives long-term remission.

15.12 DISORDERS OF PLATELETS

- **Thrombocytopenia** is decrease in platelet count. It is seen in acute infections, acute leukemia, viral infections like small pox and chicken pox, aplastic anemia, typhoid and tuberculosis.
- **Thrombocytosis** is increase in platelet count. It is seen after surgical operations and in bone fractures, also in allergic conditions, rheumatic fever and with trauma and hemorrhage. It is also seen after splenectomy.
- **Thrombocythemia** is persistent and abnormal increase in platelet count. It is seen in cancerous conditions like chronic leukemia and Hodgkin's disease.

15.13 DISORDERS OF COAGULATION

1. Disseminated Intravascular Coagulation (DIC)

DIC occurs in response to many diseases and is a pathological activation of the clotting mechanism. Small clots are formed inside the blood vessels. These clots consume proteins, clotting factors and platelets, thus disrupting the normal coagulation process leading to bleeding. Bleeding occurs from the gastrointestinal tract, surgical and injury wounds, skin and respiratory tract.

Pathophysiology DIC occurs following trauma, severe shock due to microbial infection, in acute pancreatitis, in cancer with metastasis and in premature separation of placenta when amniotic fluid enters maternal blood.

Due to these conditions, the process of coagulation and fibrinolysis gets disrupted, resulting in clotting and bleeding throughout the body.

A transmembrane glycoprotein, called **tissue factor**, is present on the surface of certain cells like macrophages, endothelial cells and monocytes. After vascular damage, it is exposed to the circulation. This now binds with the coagulation factors which triggers the coagulation mechanism.

Gram-negative sepsis triggers DIC by releasing endotoxins. When leukemia is treated, there is destruction of leukemic granulocyte precursors, which results in release of proteolytic enzymes in a large amount causing microvascular damage.

DIC can occur when circulating thrombin is in excess which combines with fibrinogen, forming multiple clots. Clots trap platelets, bigger clots are formed and microvascular thrombosis results.

Recently, studies have shown a highly expressed receptor on the surface of hepatocytes, called the Ashwell–Morell receptor, which may be responsible for thrombocytopenia in sepsis and bacteremia.This assumption remains to be proved.

2. Hemophilia

Hemophilia is a bleeding disorder with repeated episodes of prolonged and severe bleeding from any site. Joints are commonly involved. After many episodes, joints get damaged.

Pathophysiology Hemophilia is usually inherited. The disorder is passed from parents to children through the genes.

The genes that are responsible for the synthesis of clotting factors VIII and IX are carried on the X chromosome. If the female has one faulty X chromosome and the other is normal, she will be a carrier, while as the male has only one X chromosome, he will suffer from the disease if his chromosome is faulty.

There are two main forms:

Hemophilia A, where Factor VIII is abnormal and the defective gene interferes with the ability of the body to produce the normal factor and there is excessive bleeding. This type is more common than **hemophilia B,** where Factor IX is deficient resulting in deficiency of thromboplastin.

3. Von Willebrand's Disease

In Von Willebrand's disease, there are low levels of a protein called Von Willebrand factor which helps the blood to clot. This Factor also carries Factor VIII. Hence, in its deficiency, hemorrhages occur. Both males and females are equally affected while hemophilia mainly affects males. The severity is also milder than that of hemophilia. It is the most common of all inherited bleeding disorders.

REVIEW QUESTIONS

1. Describe the composition, properties and functions of blood.
2. Write the structure, properties and functions of erythrocytes.
3. Describe the stages of erythropoiesis and its regulation. Discuss the role of erythropoietin.
4. Explain the life cycle of an RBC.
5. Define ESR and its significance. How is it determined?
6. Describe synthesis, properties, functions and estimation of hemoglobin.
7. Define Landsteiner's law. Describe the different blood groups. Describe methods of determination.
8. Enumerate various clotting factors. Discuss the mechanism of coagulation of blood. Discuss factors affecting coagulation.
9. Describe synthesis and functions of leucocytes.
10. Explain the role of neutrophils in phagocytosis.
11. Write a note on the different types of WBC.
12. Describe the formation, structure and functions of platelets.
13. Write a note on the indications and complications of blood transfusion.
14. What is anemia? Discuss various types of anemias.
15. Describe various disorders of leucocytes.
16. Describe platelet disorders.
17. Write short notes on:
    a. Sickle cell anemia
    b. Phagocytosis
    c. Reticulocyte
    d. Plasma proteins
    e. Difference between RBC and WBC
    f. Hemophilia
    g. Rh factor
    h. Universal donor, universal recipient
    i. Iron deficiency anemia
    j. Megaloblastic Anemia
    k. Aplastic anemia
    l. Leukemia

Chapter

16 Reproductive System —Female, Male

- **ANATOMY OF FEMALE**
  - **Uterus**
    - Structure
    - Function
    - Support
      - Arterial supply
      - Venous drainage
      - Lymphatic drainage
      - Nerve supply
  - **Fallopian tubes**
    - Structure
    - Function
  - **Cervix**
  - **Vagina**
  - **Ovaries**
    - Structure
      - Arterial supply
      - Venous drainage
      - Lymphatic drainage
      - Nerve supply
- **PHYSIOLOGY OF FEMALE REPRODUCTIVE SYSTEM**
  - **Menstrual cycle**
    - Ovarian cycle
      - Formation and growth of Graafian follicle
      - Ovulation
      - Formation and growth of corpus luteum
      - Fate of ovum
    - Uterine cycle
      - Proliferative phase
      - Secretory phase
      - Destructive phase
    - Changes in the cervix
    - Changes in the vagina

- Mammary Glands ..... Structure
- Contraceptives ..... Various methods
  - ..... Physical methods
  - ..... Hormonal methods
- Oogenesis
- Implantation of the embryo
- Pregnancy ..... Changes ..... Signs and symptoms
  - ..... Changes in the reproductive system

• DISORDERS OF THE FEMALE SEX ORGANS

- ..... Endometriosis
- ..... Ovarian Cyst
- ..... Fibroid
- ..... Leucorrhoea
- ..... Carcinoma
- ..... Sexually transmitted diseases

• ANATOMY OF REPRODUCTIVE SYSTEM MALE

- Testis ..... Structure ..... Macroscopic
  - ..... Microscopic
  - ..... Functions
  - ..... Spermatozoa
  - ..... Undescended testis
  - ..... Ectopic testis
- Epididymis and vas deferens
- Spermatic cord ..... Applied anatomy
- Seminal vesicles
- Prostate gland
- Bulbo-urethral gland
- Penis ..... Structure

• PHYSIOLOGY

- Spermatogenesis ..... Stages of spermatogenesis ..... Stage of proliferation
  - ..... Stage of growth

- Stage of maturation
- Stage of transformation

- Factors affecting spermatogenesis
  - Role of Sertoli cells
  - Role of hormones
  - Role of other factors
- Control of spermatogenesis
- Storage of sperms
- Semen

- ○ Physiology of coitus ..... Erection, Ejaculation, Orgasm

• DISEASES OF MALE SEX ORGANS

- Epididymorchitis
- Orchitis
- Prostatic hypertrophy
- Prostate carcinoma
- Hydrocele
- Varicocele
- Testicular cancer

Introduction

Organs of the reproductive system are different in males and females.

The male reproductive system consists of testes, epididymis, vas deferens, seminal vesicle, prostate, ejaculatory duct, Cowper's (bulbo-urethral) gland and the penis.

The female reproductive system consists of ovary, Fallopian tubes, uterus (fundus, body and cervix), vagina, Bartholin's glands and breasts.

Out of these, the testes and ovaries are known as primary sex organs or gonads.

The remaining are called secondary sex organs.

Functions of Gonads

Both in males and females gonads have two functions:

1. Production of germ cell or gamete
   - male sperm
   - female ova
2. Secretion of sex hormones

In Males Testis secretes a large amount of androgen, mainly testosterone, and a small amount of estrogen.

In Females The ovary secretes a large amount of estrogens, progesterone and very small amount of testosterone.

16.1 ANATOMY OF FEMALE REPRODUCTIVE SYSTEM

The female reproductive system includes ovaries, Fallopian tubes, uterus, vagina, external genital organs and breasts.

The uterus acts as the receptacle for the male sperm. The ovaries produce the egg cells. These cells (ova) traverse the Fallopian tube to reach the uterus. Thus, the uterus is in connection with the ovaries via the Fallopian tubes. These are the internal parts of the female reproductive system.

The external organs include the labia, and the clitoris in the vulva which is connected to the vagina. The vagina is a fibromuscular tube which connects the external and internal organs of reproduction.

16.1.1 Uterus

The uterus is a pear-shaped hollow muscular organ located in the female pelvis. It is flattened antero-posteriorly, with the apex directed downward and backward.

The vesical or anterior surface is flattened and covered by the peritoneum. This surface lies just behind the urinary bladder.

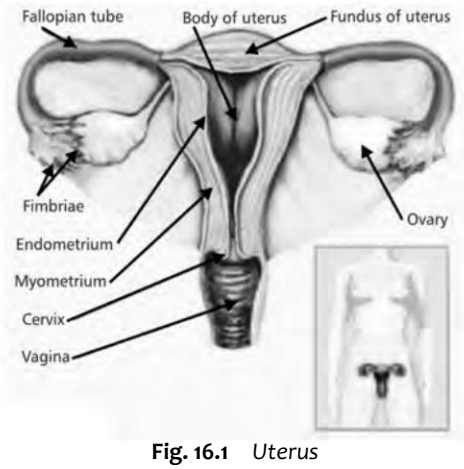


Fig. 16.1 *Uterus*

The intestinal or posterior surface is convex transversely and is also covered by the peritoneum anteriorly and posteriorly. It is in relation with the pelvic or sigmoid colon and the rectum.

Its upper part is suspended by the broad and the round ligaments, while its lower portion is embedded in the fibrous tissue of the pelvis. (See Fig. 16.2)

The uterus at its upper part measures about 7.5 cm in length, 5 cm in breadth and nearly 2.5 cm in thickness; it weighs from 30 to 40 g. On the surface, about midway between the apex and base, is a slight constriction, known as the **isthmus**, and corresponding to this in the interior is a narrowing of the uterine cavity called the internal orifice of the uterus. The portion above the isthmus is termed the body and that below is called the cervix. The part of the body which lies above a line passing through the points of entrance of the Fallopian tubes is known as the **fundus**. It is convex in all directions and is covered by the peritoneum continuous with that on the vesical and intestinal surfaces. Thus, the uterus is divided into fundus, body and cervix.

The lateral margins are slightly convex. At its upper end, the Fallopian tube pierces the uterine wall. The round ligament of the uterus is fixed below and in front of the opening of the Fallopian tube into the uterus, while behind it is the attachment of the ligament of the ovary. These three structures lie within a fold of the peritoneum which is reflected from the margin of the uterus to the wall of the pelvis, and is named the broad ligament.

1. Structure

The uterus is composed of three layers, viz.,

1. An external or serous layer
2. A middle or muscular layer
3. An internal or mucous layer

The **serous coat** is the peritoneum and covers the whole fundus, the whole of the intestinal surface and the vesical surface (only as far as the junction of the body and cervix.)

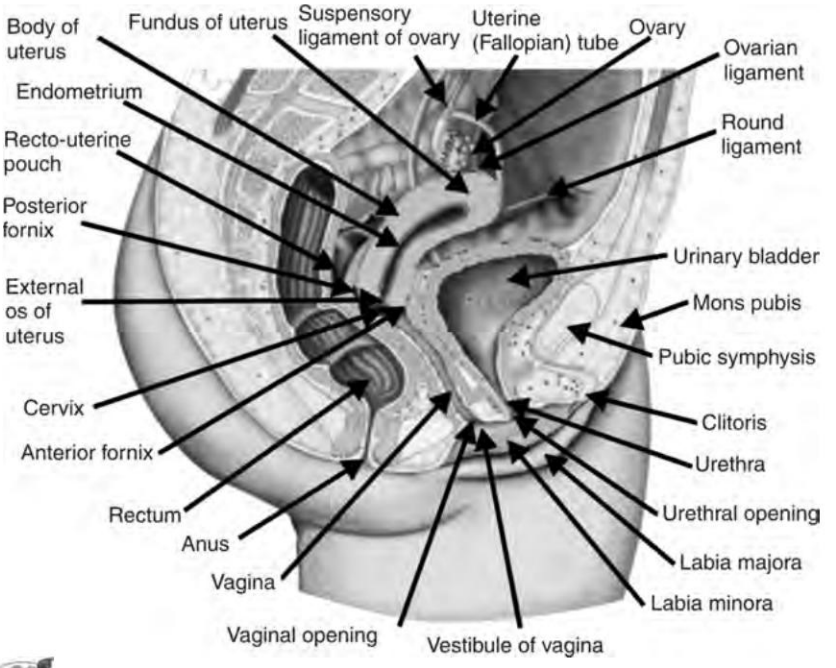


Fig. 16.2 *Female genital organs (vertical section) (Refer colour figure)*

The **muscular coat** forms the chief bulk of the substance of the uterus and is the thickest layer. It consists of bundles of unstriped muscular fibers in layers, intermixed with areolar tissue, blood vessels, lymphatic vessels and nerves.

The mucous membrane is smooth and closely adherent to the subjacent tissue. It is continuous through the fimbriated extremity of the Fallopian tubes, with the peritoneum; and, through the external uterine orifice, with the lining of the vagina.

2. Function

The reproductive function of the uterus is to accept a fertilized ovum which becomes implanted into the endometrium, and derives nourishment from the blood vessels. The fertilized ovum becomes an embryo, develops into a fetus and gestates until childbirth. The uterus undergoes changes in size and structure to accommodate itself to the needs of the growing embryo.

During the period of fertility, throughout the child-bearing period, a series of events take place every 26 to 30 days which is known as the menstrual cycle.

The uterus provides structural integrity and support to the bladder, bowel, pelvic bones and organs. It helps separate and keep the bladder in its natural position above the pubic bone and the bowel in its natural configuration behind the uterus.

3. Supports of the Uterus

The uterus is supported by eight ligaments.

They are one anterior, one posterior; two laterals or broad, two uterosacral, and two round ligaments.

The anterior ligament consists of the vesico-uterine fold of the peritoneum, which is reflected onto the bladder from the front of the uterus, at the junction of the cervix and the body.

The posterior ligament consists of the rectovaginal fold of the peritoneum, which is reflected from the back of the posterior fornix of the vagina onto the front of the rectum. They contain a considerable amount of fibrous tissue and nonstriped muscular fibers which are attached to the front of the sacrum and constitute the uterosacral ligaments.

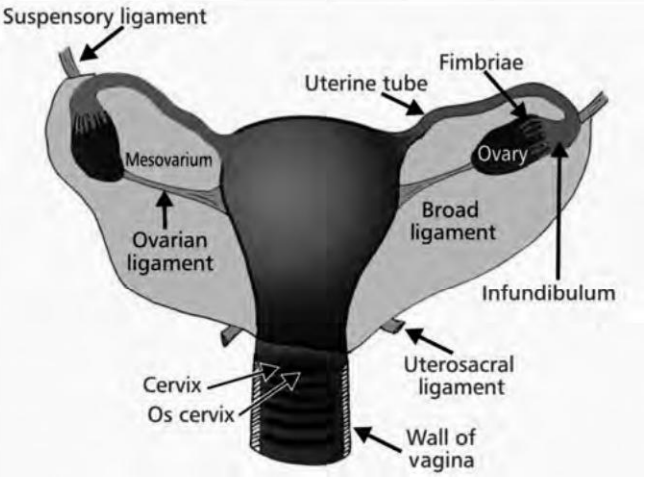


Fig. 16.3 *Uterine ligaments*

The two lateral or broad ligaments pass from the sides of the uterus to the lateral walls of the pelvis. With the uterus, they form a septum across the female pelvis, dividing that cavity

into two portions. Between the two layers of each broad ligament are the Fallopian tube, the round ligament of the uterus; the ovary and its ligament; the epoöphoron and paroöphoron, connective tissue; unstriped muscular fibers; and blood vessels and nerves.

The round ligaments are two flattened bands, 10 and 12 cm in length, situated between the layers of the broad ligament in front of and below the uterine tubes. The round ligament consists of muscular tissue, some fibrous and areolar tissue, blood vessels, lymphatics, and nerves.

(a) Arterial Supply The uterine and ovarian arteries supply the uterus. Uterine arteries arise from the hypogastric branches of the internal iliac arteries and the ovarian, from the abdominal aorta.

(b) Venous Drainage The veins correspond to the arteries. They end in the uterine plexuses and drain in the internal iliac veins.

(c) Lymphatic Drainage Deep and superficial vessels drain into the iliac blood vessels.

(d) Nerve Supply The nerves are derived from the hypogastric and ovarian plexuses, and from the third and fourth sacral nerves.

16.1.2 Fallopian Tubes

The Fallopian tubes, also known as oviducts, uterine tubes, or salpinges, are found in the pelvic cavity, running between the uterus and the ovaries on either side. They are approximately three to four inches long and are mobile. They lie between the folds of the broad ligament of the uterus. They open into the peritoneal (abdominal) cavity, very close to the ovaries. The ovarian end widens into a funnel-shaped portion called the infundibulum. It ends into multiple fingerlike projections called the **fimbriae**. One of these fimbriae is attached to the ovary. The ampulla is the widest and longest part. The isthmus is short and narrow and is attached to either side of the cornual end of the uterus.

1. Structure

The tube consists of three layers—the inner mucosal ciliated layer, which helps the ovum move from the ovary towards the uterus. The middle muscular layer with its peristaltic movements again helps the ovum move from the ovary towards the uterus. The outer layer is the serous layer.

2. Functions

The main function of the Fallopian tubes is to convey the mature ovum from the ovary to the uterus, pushing it by movements of cilia and peristaltic movements of the muscular layer. Usually, fertilization takes place in one of the tubes.

16.1.3 Cervix

The cervix is the lower, narrow portion of the uterus which joins with the top end of the vagina. It is cylindrical or conical in shape and protrudes through the upper anterior vaginal wall. Half of its length is visible while the other part lies above the vagina and cannot be seen.

16.1.4 Vagina

The vagina is a fibromuscular tubular tract leading from the uterus to the exterior of the body where it opens into the labia minora and majora. It is normally closed and widens during coitus. It remains wet due to the secretion of a lubricant fluid.

16.1.5 Ovaries

The ovary is an ovum-producing reproductive organ, found in pairs, as part of the female reproductive system.

Each ovary is a solid ovoid structure measuring about 3.5 cm long, 2 cm wide, and 1 cm thick. They are located in shallow depressions, called **ovarian fossae**, one on each side of the uterus, in the lateral walls of the pelvic cavity. The fossa usually lies beneath the external iliac artery and in front of the ureter and the internal iliac artery.

Ovaries lie within the pelvic cavity, on either side of the uterus, to which they are attached via a fibrous cord called the **ovarian ligament**. They are attached to the body wall via the suspensory ligament of the ovary. The part of the broad ligament of the uterus that covers the ovary is known as the **mesovarium**.

Ovaries lie very near to the fimbriae of the Fallopian tube. Usually, each ovary takes turns releasing eggs every month. If one ovary is absent or dysfunctional then the other ovary continues releasing eggs.

The ovaries also produce the female sex hormones, viz., estrogen and progesterone.

Before puberty, the ovaries are inactive. During childbearing years, every 28 days, one ovarian follicle matures, ruptures and releases its ovum into the peritoneal cavity. This phenomenon occurs during the menstrual cycle and is called **ovulation**.

Structure

The ovaries are covered on the outside by a layer of simple cuboidal epithelium called **germinal (ovarian) epithelium**. The visceral peritoneum envelops the ovaries. Underneath this layer there is a dense connective tissue capsule, the **tunica albuginea**. The substance of the ovaries is distinctly divided into an outer cortex and an inner medulla. The cortex appears more dense and granular due to the presence of numerous ovarian follicles in various stages of development.

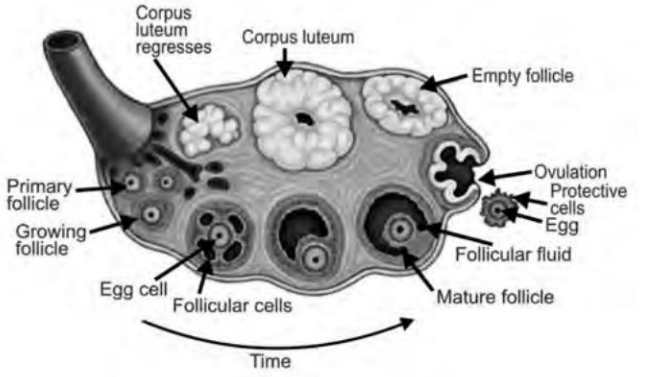


Fig. 16.4 *Various stages of development of ovarian follicle*

Each of the follicles contains an **oocyte**, the female germ cell. Also in the cortex, is the corpus luteum derived from the follicles. In between there is stroma. The medulla is loose connective tissue with abundant blood vessels, lymphatic vessels, and nerve fibers. It can be hard to distinguish between the cortex and medulla, but follicles are usually not found in the medulla. In the stroma there are immature follicles. During the period of fertility, under the influence of follicle-stimulating hormone, maturation of these primordial follicle occurs. Estrogen also stimulates maturation. Ovulation is stimulated by the luteinizing hormone.

After ovulation, the follicle, lining cells develop into the corpus luteum. The mature ovum is released into the abdominal cavity.

If the ovum is not fertilized, the corpus luteum degenerates. A new cycle starts with menstruation. Where the corpus luteum degenerates, an inactive mass of fibrous tissue is formed. This is called **corpus albicans**.

If the ovum is fertilized, it embeds itself in the wall of the uterus. It grows and develops and produces the hormone **Human Chorionic Gonadotrophin (HCG)**. This hormone stimulates the corpus luteum to continue secreting progesterone and estrogen for the first 3 months of pregnancy. The placenta then takes over this function.

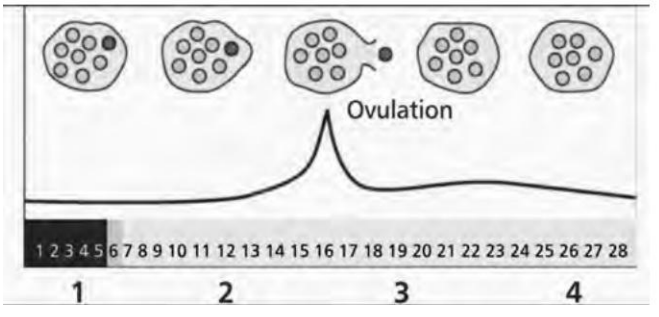


Fig. 16.5 *Process of ovulation*

Sometimes, more than one follicle matures at the same time, and thus two or more ova are released in the same cycle. This results in multiple pregnancies.

(a) Arterial Supply It is by the ovarian arteries which are branches of the abdominal aorta.

(b) Venous Drainage Veins drain into the venous plexus which drain, on the right side into the inferior vena cava and on the left side into the left renal vein.

(c) Lymphatic Drainage Lymph vessels follow the same route as the arteries and drain into the preaortic lymph nodes.

(d) Nerve Supply There is both sympathetic and parasympathetic supply. Sympathetic supply is from lumbar segments and parasympathetic supply is from sacral segments.

16.2 PHYSIOLOGY OF FEMALE REPRODUCTIVE SYSTEM

16.2.1 Menstrual Cycle

During the period of fertility, throughout the child-bearing period, a series of events take place every 26 to 30 days which is known as the menstrual cycle.

The day of menstrual cycle is identified by starting with the first day of the last menstruation.

A series of changes also takes place concurrently in the ovaries and uterine walls, stimulated by changes in the blood concentrations of hormones.

The most prominent feature is a monthly flow of blood from the uterus which is called menstruation or menses.

The menstrual cycle consists of

1. Ovarian cycle
2. Uterine cycle

1. Ovarian Cycle

The ovarian cycle consists of the following stages:

- Formation and growth of Graafian follicle
- Ovulation
- Formation and fate of corpus luteum
- Fate of ovum

(a) Formation and Growth of Graafian Follicle At the beginning of the cycle, several primordial follicles enlarge. On and about the 6th day, one of the follicles begins to grow, while others regress or remain in the normal state.

It is not known how one follicle is singled out for development.

During the development of the primordial follicle, the follicular epithelium multiplies. The central cell forms the ovum, while several layers of cells surround the ovum.

The ovum undergoes meiotic division. Both the ovum and follicle enlarge.

Droplets of fluid appear between the cells. Ultimately, a cavity is formed containing a fluid which is called **liquor folliculi**.

There are two layers of cells; a central layer which surrounds the ovum and a peripheral layer called **membrana granulosa**.

In the meantime, the stroma cells surrounding the follicle are differentiated into 2 layers.

The inner vascular layer is called **tunica vasculosa** or **theca interna**, and an outer fibrous layer is called **tunica fibrosa** or **theca externa**.

Theca interna is the vascular layer and theca externa is the layer containing thick fibers and spindle-shaped cells.

Theca interna and membrana granulosa are the chief source of estrogen.

Hormonal Control Maturation and growth of the Graafian follicle is controlled by the follicle-stimulating hormone, which is secreted by the anterior pituitary. During the process of maturation, the theca interna and membrana granulosa secrete estrogen. So from the 6th to 14th day of the cycle, the level of estrogen gradually rises in the blood.

This rising level of estrogen will inhibit the follicle-stimulating hormone and luteinizing hormone from the anterior pituitary. If pregnancy occurs, these rising levels prevent the maturation and release of another ovum.

(b) Ovulation The Graafian follicle, after becoming fully mature on around the 14th day of the cycle, ruptures and the ovum is extruded into the abdominal cavity. This process of discharge of ovum from the bursted Graafian follicle into the abdominal cavity is called ovulation. The normal ovulation time is the 14th day or + or – 4 days after the 1st day of the last menstruation.

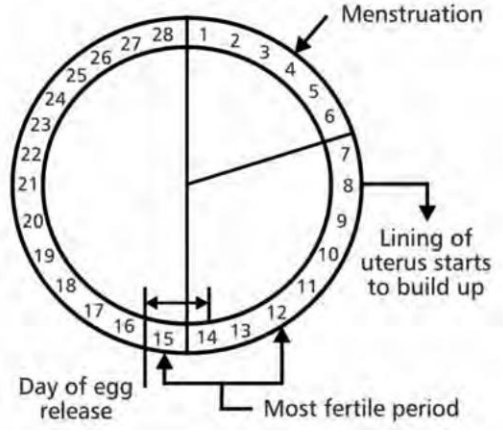


Fig. 16.6 *Calendar method of determining ovulation*

The mature Graafian follicle measures 10 mm in diameter. Gradually, it migrates towards the periphery of the ovary. As more and more liquor folliculi accumulate, pressure in the Graafian follicle increases and goes up to 15 mm of Hg.

During this period, necrosis of stigma cells and cementing substance occurs. Cells of theca interna and membrana granulose disintegrate. The ovum is discharged into the peritoneal cavity, which is surrounded by discus proligerus, along with the viscous fluid.

Hormonal Control During maturation of the Graafian follicle, constant rising level of estrogen inhibits the follicle-stimulating hormone and luteinizing hormone from the anterior pituitary through a negative feedback mechanism. But, just before ovulation, there is sudden increase (bursting) of the follicle-stimulating hormone and luteinizing hormone (mainly luteinizing hormone) from anterior pituitary which is called the 'ovulatory surge'.

There are two different opinions for bursting of follicle-stimulating hormone and luteinizing hormone.

1. Just before ovulation, a slight fall in estrogen level occurs which acts as a stimulus for sudden bursting of follicle-stimulating hormone and luteinizing hormone.
2. But, a majority believe that a sudden increase in estrogen level before ovulation beyond a particular level, instead of inhibiting follicle-stimulating hormone and luteinizing hormone, stimulates bursting of these two hormones from the anterior pituitary by a positive feedback mechanism.

The luteinizing hormone directly acts on the stigma cells and helps in ovulation.

(c) Formation and Fate of Corpus Luteum The Graafian follicle ruptures at the time of ovulation. It promptly gets filled up with blood forming **Corpus hemorrhagicum**.

The granulosa and theca cells of the Graafian follicle begin to proliferate and clotted blood is replaced by yellowish serous fluid rich in luteal cells, which is lipid in nature. This is called **corpus luteum**.

These luteal cells secrete mainly progesterone, estrogen and relaxin. If pregnancy occurs, the corpus luteum proliferates and persists. Then, there are no more menstrual cycles until after delivery.

If there is no pregnancy, the corpus luteum begins to degenerate about the 24th day of the cycle and is replaced by fibrous tissue and forms a scar called **corpus albicans**.

(d) Fate of Ovum The extruded ovum is picked up by the fimbriated end of the Fallopian tube and is transported to the body of the uterus. Usually, fertilization takes place in the Fallopian tube.

If sperms are available, fertilization occurs and the fertilized ovum is transported to the body of the uterus where it gets embedded in the wall of the uterus.

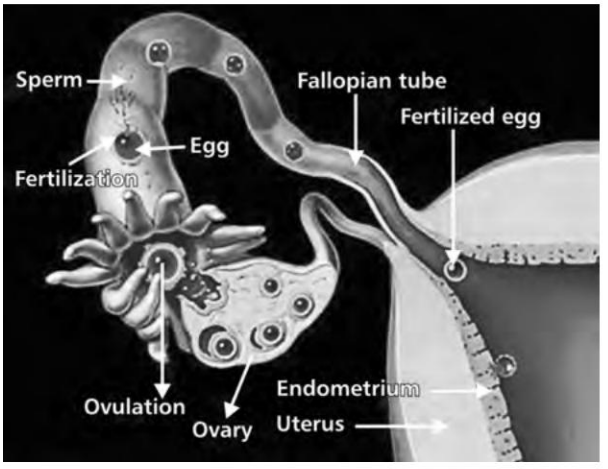


Fig. 16.7 *Fate of ovum*

If the ovum is not fertilized, it is extruded out through the vagina in 'menstruation'.

The Graafian follicle that enlarges, but fails to ovulate, also degenerates to form the **atretic follicle**.

A menstrual cycle without ovulation is called **anovulatory cycle**, which is one of the causes of sterility in females.

2. *Uterine Cycle*

Changes that take place in the uterus during the menstrual cycle are known as the uterine cycle. These changes are divided into the following phases:

- Proliferative phase
- Secretory phase
- Destructive phase or menstrual phase

(a) Proliferative Phase The proliferative phase is also known as the follicular phase or post-menstrual phase or preovulatory phase.

At the end of menstruation, all the deep layers of endometrium get washed out. Only a thin layer of the endothelial stroma remains at the base of the original endometrium.

After the 4th day, the endometrial surface begins to specialize and becomes normal. This is due to slow but gradually increasing level of estrogen from developing follicles.

From the 6th to 14th day of the cycle, the following changes are observed:

(i) Stroma and epithelial cells proliferate rapidly. So, the thickness of the endometrium increases. On the 14th day at the time of ovulation, it is 2 to 3 mm thick.

(ii) There is a progressive growth of blood vessels and hence vascularity increases.

(iii) Uterine glands increase in thickness but do not secrete anything at all or secrete a slight mucus, which guides the sperms.

Hormonal Control These changes occur under the influence of estrogen which is secreted from the developing Graafian follicle.

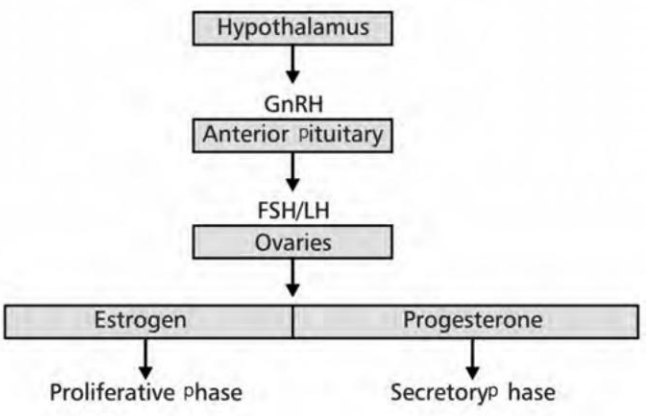


Fig. 16.8 *Hormonal control*

(b) Secretory Phase The secretory phase is also known as luteal phase, pre-menstrual phase, progestational phase or post-ovulatory phase.

This is a more constant phase and lasts from 15th to 28th day of the cycle. During this stage, the endometrium prepares itself to receive the fertilized ovum for implantation to occur.

The following changes are seen in this phase:

(i) Slight proliferation of endometrium occurs. So, towards the end of the cycle, it becomes 4–6 mm thick. This occurs under the influence of estrogen.

(ii) The endometrium becomes edematous. Cytoplasm of the stroma cells increases and there is deposition of lipid and glycogen in the stroma cells.

(iii) Actively secreting uterine glands increase in length and diameter. They become coiled and tortuous and secrete a small quantity of endometrial fluid.

(iv) Blood supply of the endometrium increases and blood vessels also become spiral or tortuous.

(v) If the ovum gets fertilized, there will be no breakdown of endometrium.The fertilized ovum will be embedded in the wall of the uterus. If the ovum is not fertilized or there is no pregnancy, the endometrium breaks down, and menstruation occurs.

Hormonal Control These changes in the endometrium are due to both progesterone and estrogen, because, during this period, the corpus luteum in the ovary begins to secrete estrogen and progesterone. Progesterone further inhibits the maturation of the Graafian follicle by inhibiting the follicle-stimulating hormone and lutetinizing hormone.

(c) Destructive Phase The destructive phase is also known as the menstrual phase.

Placental gonadotrophins are essential for further growth of the corpus luteum. In the absence of pregnancy, the placenta

will not be formed. Hence, the corpus luteum regresses due to lack of support of oestrogen and progesterone. As a result the following changes are observed:

(i) Spiral arteries in the uterine wall constrict. Ischemia occurs in the superficial layer of endometrium.
(ii) The basal layer remains intact. Due to ischemia, necrosis of superficial layer occurs.
(iii) The walls of the arteries are weakened. Damaged tissue liberates anticoagulants.
(iv) When constriction of spiral arteries is relieved, they dilate. Their damaged walls rupture producing hemorrhage which is called menstrual flow.

Sloughing is facilitated by progesterone released from the endometrium. Menstrual flow is predominantly arterial. Only 25% of blood is from the veins. It consists of secretions from endometrial glands, endometrial cells, unfertilized ovum and blood coming from the broken capillaries.

Unless the flow is excessive, it does not contain clots.

Bleeding stops when spiral arteries again constrict and the endometrium regenerates from basal layer.

The average duration of menstrual flow is 5 days.

3. Changes in the Cervix

The mucosal layer of the cervix also shows cyclical changes during different phases of the menstrual cycle.

Estrogen (proliferative phase) makes the cervical mucosa thin and alkaline which promotes survival and transport of sperm.

Progesterone (secretory phase) makes it thick, cellular and tenacious.

Cervical mucosa is thinnest at the time of ovulation. When it gets dried up, it forms a crystalline pattern.

During pregnancy, it becomes thick.

4. Changes in the Vagina

Under the influence of estrogen, the vaginal epithelium becomes cornified. This occurs during the proliferative phase.

Under the influence of progesterone, thick mucus is secreted from the vaginal epithelium.

The epithelium proliferates and gets infiltrated with white blood cells. These changes are seen during the secretory phase.

16.2.2 Mammary Glands (Breast)

Mammary glands are accessory glands of the female reproductive system. They are milk-producing glands and are present in a rudimentary and generally nonfunctional form in males. Mammary glands are regulated by the endocrine system and become functional in response to the hormonal changes associated with pregnancy.

Externally, each breast has a raised nipple, which is surrounded by a circular pigmented area called the **areola**.

Mammary glands are probably highly modified sweat glands. At birth, they are rudimentary. At puberty, they start developing under the influence of hormones. Increasing levels of estrogen stimulate the development of glandular tissue in the female breast. Estrogen also causes the breast to increase in size through the accumulation of adipose tissue. Progesterone stimulates the development of the duct system.

During pregnancy, these hormones enhance further development of the mammary glands. **Prolactin**, from the anterior pituitary, stimulates the production of milk within the glandular tissue, and **oxytocin** causes the ejection of milk from the glands by a positive feedback mechanism.

Structure

Each lobe consists of about 20 lobes of glandular tissue. The basic components of the mammary gland are the alveoli lined with milk-secreting cuboidal cells and surrounded by myoepithelial cells. These alveoli join up to form groups known as lobules, and each lobule has a lactiferous duct that drains into openings in the nipple.

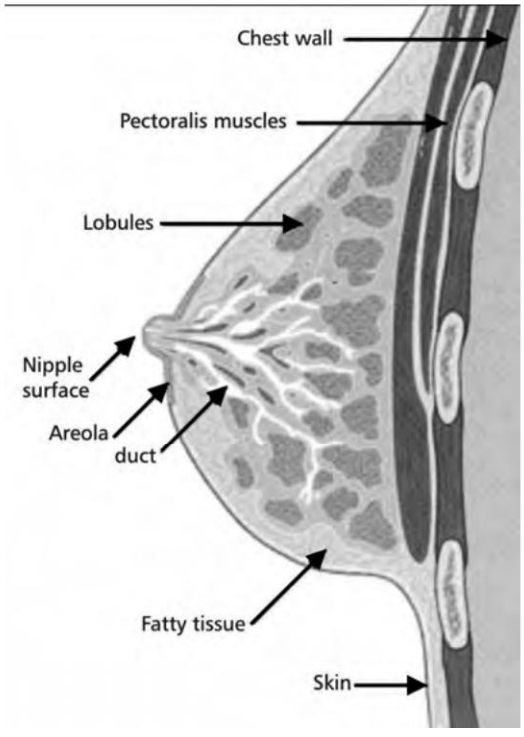


Fig. 16.9 *Structure of the breast*

The lactiferous ducts form dilatations before they open into the nipple.

Fibrous tissue supports the glandular tissue. A fat layer covers the gland surface.

The nipple is more or less at the center of the breast, is conical in shape and protruding from the breast surface. It is surrounded by a pigmented area called the areola. There are many sebaceous glands on its surface which lubricate the nipple during lactation.

Blood is supplied to the breast through the axillary, intercostal and internal thoracic vessels.

The nerve supply is from branches of the fourth, fifth, and sixth intercostal nerves.

The mammary gland of a woman who has not borne children consists of a conical disk of glandular tissue, encased in fat that gives the breast its shape. The gland is made up of lobes drained by separate ducts which meet at the nipple. Pregnancy causes the cells lining the lobes to multiply, and lactation begins in response to hormones released at the time of birth. At the end of lactation, the glands return, almost, to the original state as it was before pregnancy. After menopause, they atrophy and are largely replaced by connective tissue and fat.

The main function of the mammary gland is to produce milk after delivery (child birth). Prolactin stimulates lactation. They are active only during late pregnancy and after delivery.

16.2.3 Contraceptives

Birth control is synonymous with contraception. Contraception refers to mechanisms that are intended to reduce the likelihood of a sperm cell fertilizing the egg and thereby reducing the likelihood of pregnancy. Birth control is commonly used as part of family planning.

1. Various Methods

There are many different types of contraception available.

(a) Pill It is a tablet containing two female hormones—an estrogen and progestogen.

These two hormones stop ovum production each month and hence there is no pregnancy. In addition, the hormones thicken the secretions round the cervix, making it difficult for sperm to get through.

(b) Intrauterine Device (IUD) Most IUDs are T-shaped. They are made of plastic and copper, sometimes with a little silver inside. They act in three main ways:

- They prevent the sperm from getting through the uterus into the tubes.
- They alter the secretions (mucus) in the cervix, creating a further barrier for sperm.
- They affect the uterus lining, making it less likely to accept the egg.

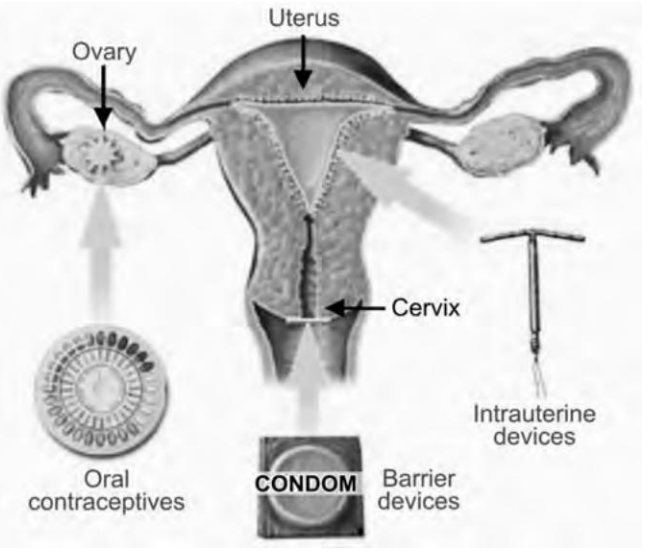


Fig. 16.10 *Various devices for contraception*

(c) Intrauterine System (IUS) The IUS is quite different from the IUD, because it contains a hormone. In addition to being a contraceptive, it usually makes the periods shorter, lighter and pain-free. So it is often used to treat period problems.

(d) Implants An implant is put under the skin in the forearm. From its position under the skin, it releases a steady stream of the female-type hormone **etonogestrel** into the bloodstream. The hormone reaches the ovaries and prevents them from releasing eggs. It also causes some minor anti-conception changes in the uterus lining and in the cervix. The chances of pregnancy are very small. Its use is not very frequent as its side effects are not known.

(e) Injections They are very efficient. They stop ovulation and thicken the mucus in the cervix, making it difficult for sperm to get through. They make the lining of the uterus thinner, so that if an ovum became fertilized, it would have difficulty attaching itself to the lining.

(f) Contraceptive Patch It is a sticky patch put on the skin, and it releases two hormones that stops pregnancy. It is light pink in color and 2 inches by 2 inches (5 cm by 5 cm) in size.

(g) Diaphragms and Caps There are two types of contraceptive caps:

- The diaphragm
- The cervical cap

A diaphragm is bigger than a cervical cap. It is placed into the vagina before sex, positioning it so that it prevents the sperms from reaching the cervix.

A cervical cap is much smaller. It is placed directly onto the cervix, so as to stop sperm getting in. Cervical caps are much less commonly used than diaphragms.

(h) Chemical Contraceptives Spermicides (chemicals which destroy sperms) were quite widely used until recently.

Foams are inserted into the vagina with a special applicator, immediately before sex.

Vaginal tablets (pessaries), gels, jellies and creams are mainly intended for spreading onto contraceptive diaphragms or caps before insertion. **Films** are very rarely used nowadays. **Sponges** containing spermicides are also rarely used.

(i) Morning-after Pill It stops pregnancy if contraception fails or care for contraception was not taken. It prevents the ovaries from releasing an egg and alters the lining of the uterus, so that a fertilized egg cannot embed itself there.

(j) Condoms There are two types of condoms: male and female. The **male condom** is also known as a sheath, made of thin latex—a form of rubber. The **female condom** is a round ring at the opening end and another one at the closed end, which is the end that goes into the top of the vagina. It is made of polyurethane.

(k) Coitus Interruptus It is also known as **withdrawal method**. It is still very widely used—particularly by young couples, or by people who do not want to use medical methods of contraception, where the semen is ejected outside the vagina.

(l) Sterilization for Women It means preventing the woman from becoming pregnant by means of an operation in which the Fallopian tubes are blocked or cut through—this makes it difficult for the eggs to reach the uterus. (See Fig. 16.1)

The Fallopian tubes (where the egg is fertilized by the sperm) are blocked by surgery or ligated. Both the tubes are operated. In recent years, it has become much more common to do the procedure by the laparoscopic method.

(m) Vasectomy for Men Vasectomy is done on both the sides, where the vas deferens is cut/ligated. It is simpler than sterilization of women and is almost always done as an outpatient procedure. It stops the sperm entering the semen and is a permanent form of contraception.

Another way of classifying contraceptives is as follows:

2. *Physical Methods*

Physical methods work in a variety of ways. They physically prevent sperm from entering the female reproductive tract; hormonally prevent ovulation from occurring, making the woman's reproductive tract not acceptable to the sperm or surgically altering the male or female reproductive tract to induce sterility. Physical methods, e.g., sterilization vary in simplicity, convenience and efficacy.

Barrier methods, e.g., condoms and cervical barriers, place a physical impediment to the movement of sperm into the female reproductive tract.

Spermicide creates a chemical barrier. Spermicides may be used alone, or in combination with a physical barrier.

3. *Hormonal Methods*

There are a variety of delivery methods for hormonal contraception.

Combinations of synthetic estrogen and progestin are commonly used. These include the combined oral contraceptive pill, the patch, and the contraceptive vaginal ring.

Other methods contain only a synthetic progestogen. These include the progesterone—only pill, the injectables Depo Provera given as an intramuscular injection every three months and Noristerat given as an intramuscular injection every 8 weeks, and contraceptive implants.

The only forms of contraceptives currently available to men are condoms, the withdrawal method and vasectomy. Other forms of male contraception are in various stages of research and development.

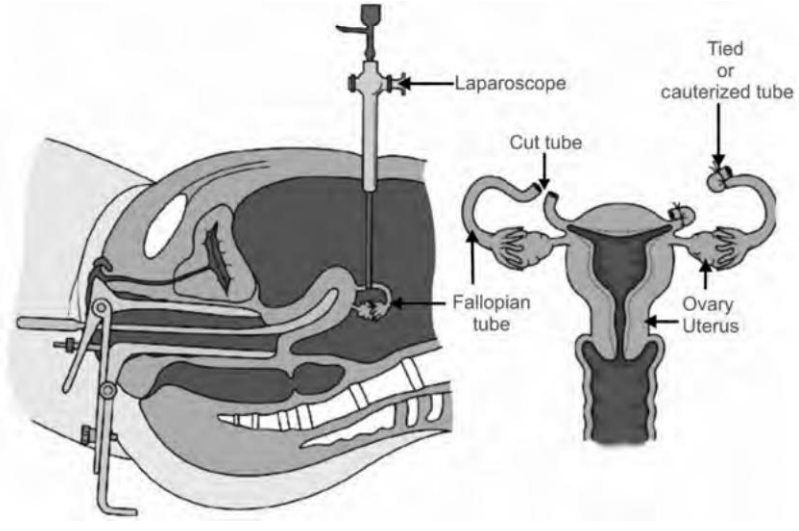


Fig. 16.11 *Tubal sterilization laparoscopy*

A male hormonal contraceptive combination protocol has been developed, involving injections of Depo Provera to prevent spermatogenesis, combined with the topical application of testosterone gel to provide hormonal support.

A male contraceptive pill that releases testosterone over three months is a potentially safe and practical method of contraception.

The rhythm method (with a rather high failure rate of ten per cent per year) was developed in the early 20th century, as researchers discovered that a woman only ovulates once per menstrual cycle. It is not totally effective.

16.2.4 Oogenesis

Oogenesis is the formation and maturation of an ovum. It is the female equivalent of the male process of gametogenesis. Spermatogenesis begins at puberty while oogenesis begins even before the birth of the female child. It involves the development of the various stages of the immature ovum. (See Fig. 16.12)

The primitive germ cells originate from the yolk sac. They undergo a number of mitotic divisions and differentiate into the primary oocyte. The primary oocyte is surrounded by a single layer of follicular cells and this entire structure is called the **primordial follicle**.

At puberty, between 4 to 10 follicles begin to develop but only 1 or 2 are released. Each oocyte finishes its first meiotic division, to form a secondary oocyte and polar body. It begins the next meiosis cycle and is arrested in its second metaphase, at which point it is released from the ovary. The final maturation occurs only after fertilization by the sperm in the Fallopian tube completing the second meiotic division. (See Fig. 16.13 on next page)

Two daughter cells are formed, each having 23 chromosomes. The larger one is called **mature ovum**, and the smaller one is the **second polar body**. In the absence of fertilization, the secondary oocyte does not complete the second meiotic division and degenerates.

A fully mature ovum is the largest cell of the body. It consists of a cell membrane called vitelline membrane, cytoplasm, and an eccentrically situated nucleus (23 chrosomes), with a nucleolus. Outside the cell membrane is a transparent mucoprotein membrane called **zona pellucida**. Between the zona pellucida and vitelline membrane is a narrow space called the **perivitalline space**.

16.2.5 Implantation of the Embryo

Implantation is an event that occurs early in pregnancy. The embryo loosely attaches to the endometrium of the uterus on the anterior or posterior wall of the body of the fundus 6 days after fertilization. (See Fig. 16.14 on next page)

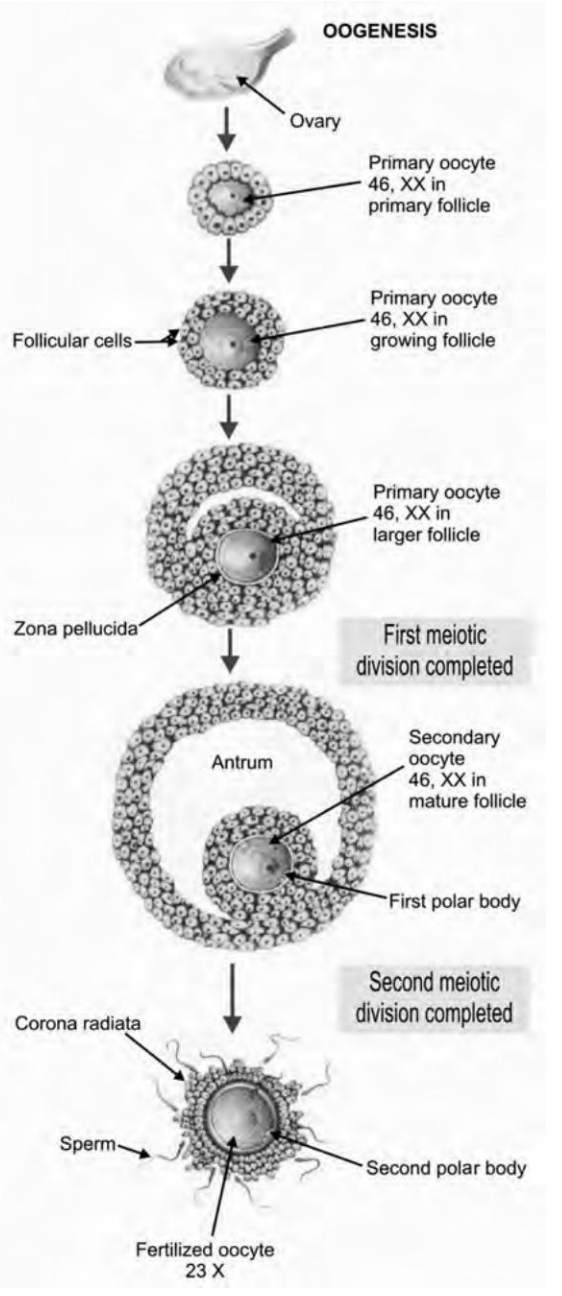


Fig. 16.12 *Oogenesis*

The endometrium is in the secretory phase at this time. Its surface produces rounded cells, which cover the whole area. These cells are called **decidual cells** and the endometrium is now known as **decidua**. That part of the decidua which is between the embryo and stratum basalis is called **decidua basalis**. It provides glycogen and lipids to the developing embryo and fetus and it later on becomes the maternal part of the placenta. The portion of the decidua between embryo and uterine cavity is called the **decidua capsularis**. The **decidua parietalis** is the remaining part of the endometrium which is

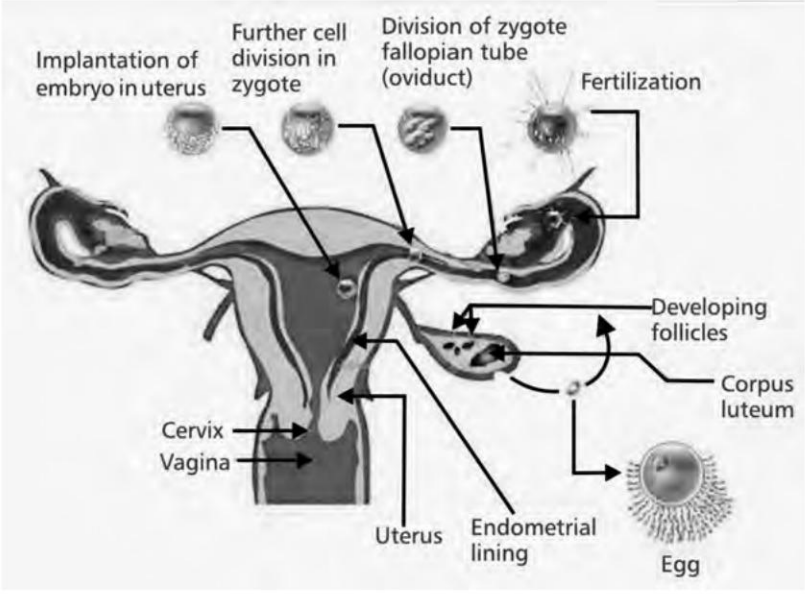


Fig. 16.13 *A section through the Fallopian tube and uterus showing the sequence from fertilization to Implantation*

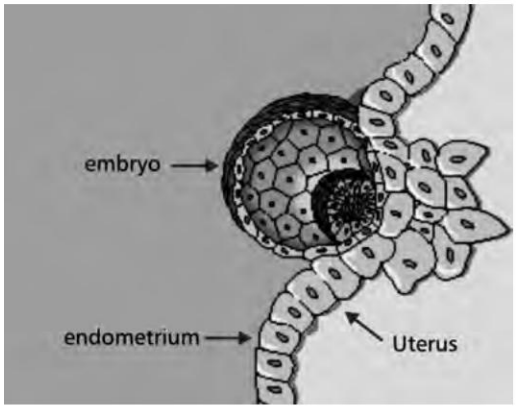


Fig. 16.14 *Embryo implants in uterus*

not involved in implantation. As the fetus enlarges, the decidua capsularis fuses with the decidua parietalis because it bulges into the uterine cavity. The uterine cavity gets obliterated. At 27 weeks, the decidua capsularis degenerates.

After **implantation,** the decidua remains through the first trimester of pregnancy. It is then replaced by the definitive placenta. However, some elements of the decidualization remain throughout pregnancy.

16.2.6 Pregnancy

When the ovum is fertilized, pregnancy occurs. Pregnancy lasts for about 40 weeks, counting from the first day of the last normal menstrual period.

1. Changes During Pregnancy

The changes that occur in the pregnant female's body are caused by several factors. Many of these changes are the result of hormonal influence, some are caused by the growth of the fetus inside the uterus, and some are the result of the woman's physical adaptation to the changes that are occurring.

The weeks are grouped into three trimesters.

2. Signs and Symptoms of Pregnancy

- **Amenorrhea**—The stoppage of the menstrual periods is a definite indication of pregnancy.
- **Morning sickness**—It is usually present during the 1st pregnancy and appears following the missed period and lasts up to 3 to 4 months.
- **Frequency of micturition** is usually seen during 8 to12 weeks of pregnancy. It is due to pressure of the uterus on the fundus of the bladder. Congestion of the bladder mucosa is also contributory.
- Change in maternal osmoregulation results in thirst and polyuria.
- Fatigue
- The breast enlarges between 6 to 8 weeks and gives rise to discomfort in the form of heaviness and fullness.
- Perception of active fetal movements by the mother is felt at about the 18th week. The subjective symptoms such as nausea, vomiting and frequency of micturition subside.
- Palpation of fetal parts can be made out by the 20th week.
- Fetal heart sound is the most conclusive clinical sign of pregnancy and can be heard with a stethoscope.
- Lightening occurs at about the 38th week—a sense of relief of the pressure symptoms due to engagement of the presenting part.
- Frequency of micturition reappears.

- Fetal movements are visible and they also become more pronounced.

3. Changes in the Reproductive System during Pregnancy

Changes are most obvious in the organs of the reproductive system during pregnancy.

(a) Uterus The capacity of the uterus must expand to accommodate a seven-pound fetus and the placenta, the umbilical cord, 500 mL to 1000 mL of amniotic fluid, and the fetal membranes.

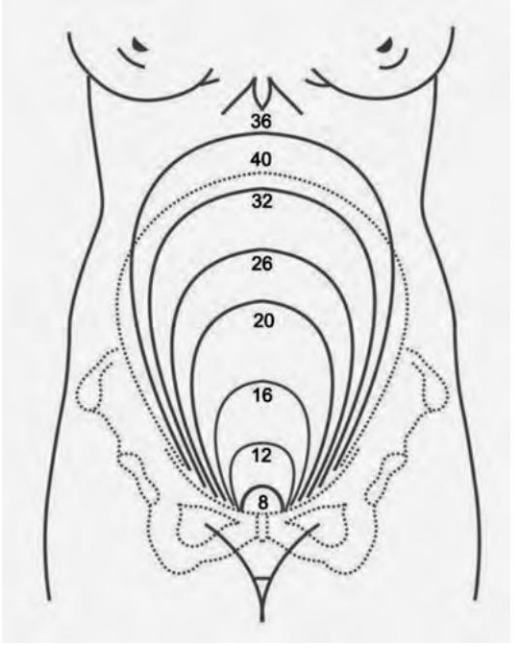


Fig. 16.15 *Approximate height of the fundus at various weeks of pregnancy*

The abdominal contents are displaced to the sides as the uterus grows. Growth of the uterus occurs at a steady pace. The size of the uterus usually reaches its peak at 38 weeks of gestation. The uterus may drop slightly as the fetal head settles into the pelvis, preparing for delivery.

(b) Cervix The cervix undergoes a marked softening. A mucus plug is formed in the cervical canal. This is the result of enlarged and active mucus glands of the cervix. It serves to seal the uterus and to protect the fetus and fetal membranes from infection. The mucus plug is expelled at the end of the pregnancy. This may occur at the onset of labor or precede labor by a few days. Softening of the cervix occurs prior to the beginning of labor.

(c) Vagina Increased circulation to the vagina early in pregnancy changes the color from normal light pink to a purple hue.

(d) Ovaries The Follicle-Stimulating Hormone (FSH) ceases its activity due to the increased levels of estrogen and progesterone secreted by the ovaries and corpus luteum. The FSH prevents ovulation and menstruation.

The corpus luteum enlarges during early pregnancy and may even form a cyst on the ovary. The corpus luteum produces progesterone to help maintain the lining of the endometrium in early pregnancy. It functions until about the 10th to 12th week of pregnancy when the placenta is capable of producing adequate amounts of progesterone and estrogen. It slowly decreases in size and its function also decreases after the 10th to 12th week.

16.3 DISORDERS OF THE FEMALE SEX ORGANS

1. Endometriosis

The presence of the functioning endometrium in sites other than uterine mucosa is called endometriosis. Common sites are abdominal, extra-abdominal and remote.

In the abdomen it may be seen in relation to the ovary, pouch of Douglas, ligaments, rectovaginal segment, rectum and pelvic nodes.

Extra-abdominal sites are abdominal scar after surgery (e.g., tubectomy, episiotomy scar), umbilicus, vagina and cervix.

Remote sites are pleura, lungs, and deep tissues of arms and thighs.

Pathophysiology It is still unclear and many theories are put forward:

- **Retrograde Menstruation**—Retrograde flow of menstrual blood takes place and endometrial fragments get implanted at pelvic and peritoneal sites. Retrograde menstruation *per se* cannot produce endometriosis. A genetic factor or hormonal influence also works for implantation and growth of endometrial fragments. This theory does not explain implantation at distant sites.
- **Celomic Metaplasia**—Chronic irritation of the pelvic peritoneum by the menstrual blood can lead to celomic metaplasia and result in endometriosis. This explains endometriosis of abdominal viscera, umbilicus and rectovaginal septum.
- **Vascular Theory**—This explains endometriosis at the lungs, arms or thighs.
- **Genetic and Immunological Factors**—Genetic basis is in less than 10%. A defect of local cellular immunity probably is responsible for ectopic deposits.

Thus, endometriosis cannot be described on any one theory.

2. Ovarian Cyst

An ovarian cyst is a fluid-filled sac surrounded by a very thin wall which develops in an ovary. Any ovarian follicle that is larger than about two centimeters is termed an ovarian cyst. An ovarian cyst can be as small as a pea, or larger than an orange.

Most ovarian cysts are benign (noncancerous) and cause no symptoms. Some cause problems such as pain and irregular bleeding.

Ovarian cysts affect women of all ages. They occur most often, however, during a woman's child-bearing years and in up to 14% of post-menopausal women.

Many small ovarian cysts will resolve and disappear over a few months. Removal of an ovarian cyst may be advised, especially if there are symptoms or if the cyst is large.

3. Fibroid

A fibroid is not only the commonest benign tumor of the uterus but is the commonest benign solid tumor in females.

It originates from the smooth muscle layer and the accompanying connective tissue of the uterus. Fibroids are found during the middle and later reproductive years and most are asymptomatic. They can grow and cause heavy and painful menstruation, painful sexual intercourse, and urinary frequency and urgency. Fibroids are often multiple in occurrence.

A small lesion can be symptomatic if located within the uterine cavity, while a large lesion outside the uterus may go unnoticed.

They could be the following:

- **Intramural fibroids,** which are located within the wall of the uterus and are the most common type.
- **Subserosal fibroids,** which are located underneath the mucosal (peritoneal) surface of the uterus and can become very large.
- **Submucosal fibroids,** which are located in the muscle beneath the endometrium of the uterus and distort the uterine cavity, and even a small lesion in this location may lead to bleeding and infertility.
- **Cervical fibroids** are located in the wall of the cervix (neck of the uterus).

Fibroids, particularly when small, may be entirely asymptomatic.

Symptoms depend on the location of the lesion and its size which include heavy or painful periods, abdominal discomfort or bloating, painful defecation, backache, urinary frequency or retention and in some cases, infertility. There may also be pain during intercourse, depending on the location of the fibroid. During pregnancy, they may be the cause of miscarriage, bleeding, premature labor, or interference with the position of the fetus.

Most cases of fibroids are managed by 'watchful waiting' which includes periodic sonographic assessment.

The presence of symptomatic uterine fibroids can be solved by surgery. Surgical removal of a uterine fibroid usually takes place via hysterectomy, in which the entire uterus is removed, or myomectomy, in which only the fibroid is removed.

4. Leucorrhea

Leucorrhea is defined as increase in the normal whitish discharge from the vagina. There is more discharge at puberty, when the sexual functions are becoming established

It often occurs normally but if excessive may be a symptom of infection. It may be thick, viscid and foul smelling.

Leucorrhoea can be classified as cervical leucorrhoea or vaginal leucorrhoea, i.e., according to the place of its origin—cervix or vagina.

Pathophysiology The physiological basis is dependent on the endogenous estrogen level for normal vaginal secretion. With the rising estrogen level, there is abundant secretory activity of the endocervical glands and hence the superficial vaginal epithelium becomes rich in glycogen. The glycogen-loaded epithelium sheds and the glycogen is converted into lactic acid by the Doderlein bacilli. The pH becomes acidic.

Causes Excess secretion could be due to

- Physiological excess
- During puberty: due to increased level of endogenous estrogen
- During menstrual cycle: due to rise in estrogen
- It is also increased during pregnancy due to hyperoestrinism.
- Increased secretion is also seen with sexual excitement.
- **Cervical causes**—Cervical erosion, chronic cervicitis, mucous polyp are causes for excess secretion.
- Vaginal causes—Uterine prolapse, chronic pelvic inflammation, use of the pill can cause increased vaginal transudation.

Treatment The most important factor in treatment is increasing the general health of the patient. Relieving her anxiety and maintaining a sympathetic attitude towards the patient is necessary. Cervical lesions require surgical treatment. Pelvic lesions and infections have to be treated medically. Pill users have to stop taking the pill temporarily. Above all, local hygiene has to be maintained.

5. Carcinoma

(a) Carcinoma of the Cervix Carcinoma of the cervix is the most common malignancy of the female genital tract. Dysplasia is the earliest form of pre-cancerous lesion. The site of lesion is 80% in the ectrocervix and 20% in the endocervix. It starts with dysplasia and there is change in the shape, growth and number of cervical cells. The cells usually progress to cancer.

The commonest variety is squamous cell carcinoma, either well differentiated or poorly differentiated. In most cases, it is detected early by the Pap test. Some consider it due to the virus that causes genital warts. The risk is more with more sexual partners. Some consider cigarette smoking to have some relation to it. Intercourse at a young age could also be contributory.

(b) Ovarian Cancer Ovarian cancer constitutes 5% of genital malignancy and is the main cause of death among all gynecological malignancies. The cause is obscure. Probably there is some relation to nulliparity and pregnancy after 30. Repeated pregnancies could have a protective effect. Combined steroid contraceptive pills could give protection. Cosmetic talc which is contaminated with asbestos and used with condoms has been implicated. It has been found that females working in asbestos-related industries have a tenfold risk of getting ovarian cancer. Heredity may play a role. Risk factors also include age, as seen after fifty, and occurs more in whites.

In the early stages, there may be no symptoms or only mild abdominal discomfort, nausea, loss of appetite and flatulence. In later stages, there appears a large abdomen, abdominal pain, menstrual abnormalities, urinary symptoms, gastrointestinal disturbances and severe menstrual bleeding.

6. *Sexually Transmitted Diseases*

Sexually Transmitted Diseases (STD) are infections that are transferred from one person to another through sexual contact. There are more than 25 diseases that are transmitted through sexual activity. Other than HIV, the most common STDs are chlamydia, gonorrhea, syphilis, genital herpes, hepatitis B, trichomoniasis, and bacterial vaginosis. Young adults aged 15 to 24 are at the greatest risk for acquiring an STD.

(a) Chlamydia The causative organism is **Chlamydia trachomatis**. There are often no symptoms; hence those who are infected may unknowingly pass the disease on to their sex partners. Women may experience abnormal vaginal discharge and a burning sensation while passing urine. Men may have discharge from the penis and a burning sensation while urinating. Treatment for this curable infection generally involves a course of antibiotics. This condition is responsible for pelvic inflammatory disease. Uterine tubes can get inflamed and infertility may occur due to healing by the formation of a scar.

(b) Gonorrhea The responsible organism is **Neisseria gonorrhoeae**. The infection is transmitted from one person to another through vaginal, oral, or anal sexual relations. It occurs mostly in persons between 15 to 30 years.

In males, there is a yellowish discharge from the penis, associated with painful, and sometimes frequent, urination. Some of the infected men have no symptoms. The infection may move into the prostate, seminal vesicles and epididymis, causing pain and fever. Untreated gonorrhea can lead to sterility.

Some women with gonorrhea may have no symptoms. Early symptoms may include a discharge from the vagina, discomfort in the lower abdomen, irritation of the genitals, pain or burning during urination and abnormal bleeding. The infection will usually spread to the uterus, Fallopian tubes, and ovaries, causing pelvic inflammatory disease, giving lower abdominal pain, bleeding between menstrual periods, vomiting, or fever. If untreated, it can lead to severe complications.

Rarely the infection can pass to the fetus during the passage of a newborn through the birth canal. It is transmitted to the eyes which could cause blindness. Instillation of 1% silver nitrate solution can prevent infection.

(c) Syphilis Syphilis is caused by *Treponema pallidum*. The route of transmission of syphilis is almost always through sexual contact, although rarely there could be transmission from mother to child *in utero*.

Different manifestations occur depending on the stage of the disease.

Primary syphilis is acquired via direct sexual contact with the infectious lesions of a person with syphilis. The chief lesion is a skin lesion at the point of contact, which is usually the genitalia (penis, vagina or rectum), called a **chancre** which is a firm, painless skin. The lesion may persist for 4 to 6 weeks and usually heals spontaneously.

Secondary syphilis occurs 1–6 months after the primary infection. There may be a reddish-pink rash on the trunk and extremities. The rash can involve the palms of the hands and the soles of the feet. Other symptoms include fever, sore throat, malaise, pain in the joints and muscles, weight loss, headache, and enlarged lymph nodes. Infection spreads to the major systems of the body, leading to organ degeneration.

The **tertiary stage** is characterized by the formation of soft, tumorlike balls of inflammation known as granulomas. There is neuropathic joint disease, which is a degeneration of joint surfaces resulting from loss of sensation and fine position sense (proprioception). The more severe manifestations include neurosyphilis and cardiovascular syphilis. Finally, the patients become bedridden. Damage to cerebral cortex can lead to memory loss, irritability and behavior changes.

(d) Genital Herpes Genital herpes is caused by the herpes simplex viruses (type 1 or type 2). Most genital herpes is caused by HSV-2. There appear as one or more blisters on or around the genitals or rectum. The blisters break, leaving tender ulcers (sores) that may take two to four weeks to heal. Another outbreak can appear weeks or months after the first. The blisters appear and disappear but the virus remains in the body indefinitely. Recurrences occur many times a year.

16.4 ANATOMY OF MALE REPRODUCTIVE SYSTEM

As mentioned earlier, the male reproductive system consists of testes, epididymis, vas deferens, seminal vesicle, prostate, ejaculatory duct, Cowper's (bulbo-urethral) gland and the penis.

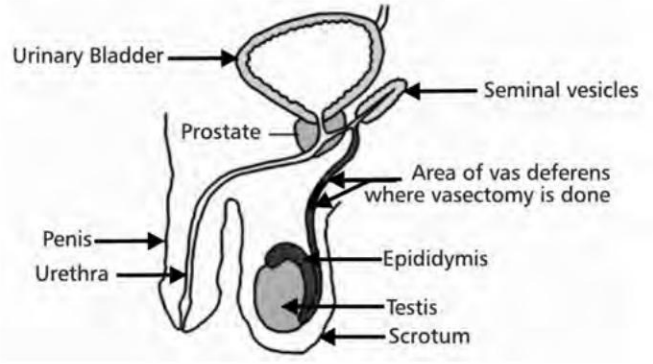


Fig. 16.16 *Male reproductive system (schematic)*

16.4.1 Testes

A testes is one of the pair of male gonads that produces sperms and stores them.

The testes lie within the scrotum, outside the abdominal cavity.

The testicles form inside the abdomen of the male fetus, between 25 and 35 weeks of gestation. The baby's testicles descend down, through the inguinal canal, to the lower abdomen and settle into the scrotum during the last 2 months of fetal development. As the internal body temperature is too high to produce viable sperms, this descent is essential.

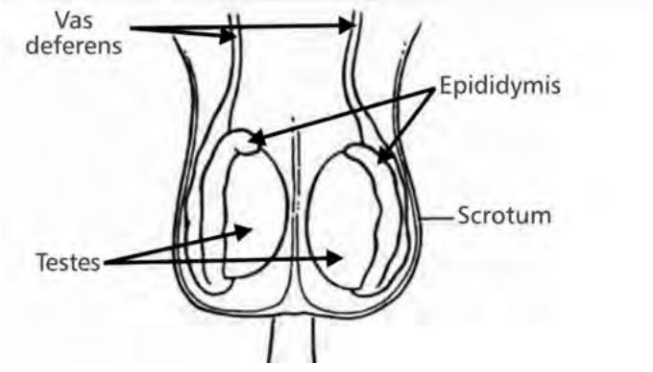


Fig. 16.17 *Testes in scrotum*

1. Structure

Blood Supply The testes are supplied with blood by the two internal spermatic arteries.

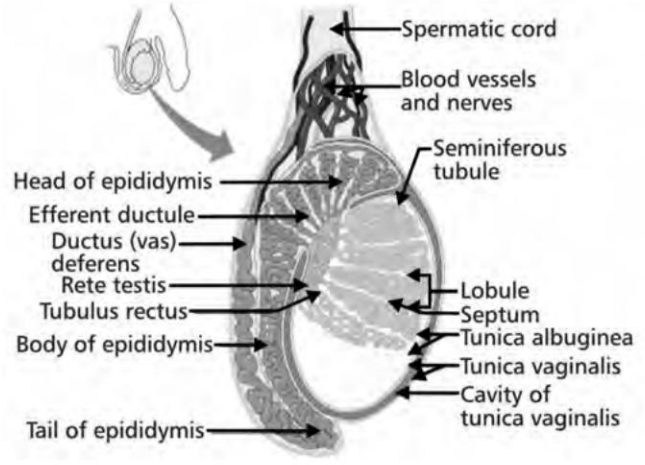


Fig. 16.18 *Structure of testis*

Venous Drainage Blood is drained by the testicular veins that form the pampiniform plexuses constituting the greater part of the spermatic cords.

Nerve Supply They are innervated by the spermatic plexuses of nerves from the celiac plexuses of the autonomic nervous system.

(a) Macroscopic The scrotum is a sac that lies under the penis and in front of the anus. It is divided internally into two halves by a membrane; each half containing a testis. The base of the scrotum becomes covered with curly pubic hairs at puberty. The scrotum is homologous to the labia majora in females. The function of the scrotum is to keep the testes at a temperature slightly lower than that of the rest of the body. The scrotal bags help the testes to ascend or descend into and out of the body.

The scrotum has an outer layer of thin, wrinkled skin over a layer of tissue which contains a muscle called the **dartos muscle**. The other coverings are the external spermatic fascia (the cremasteric layer), the internal spermatic fascia, and the tunica vaginalis which is a downgrowth of the abdominal and pelvic peritoneum. Beneath the tunica vaginalis layer is a fibrous layer called **tunic albuginea**, which sends partitions of fibrous tissue and divides the glandular part of the testes into sections or lobes. The **tunica vasculosa** is a layer consisting of a network of capillaries in a delicate connective tissue.

Each testis is a laterally compressed oval body about 4 cm long and 2.5 cm wide and weighs about 12 g. It lies obliquely in the scrotum, with the upper end directed ventrally and slightly laterally and the lower end directed dorsally and slightly medially. The anterior border, lateral surfaces, and poles of the organ are convex, free, smooth, and covered by the tunica vaginalis.

(b) Microscopic Each testis consists of several hundred conical lobules containing approximately 900 tiny coiled

seminiferous tubules, each about 75 mm long, in which spermatozoa develop. Each seminiferous tubule has a germinal layer peripherally. Various stages of spermatogenesis are seen centrally with spermatozoa in the center. More peripherally are spermatids, secondary spermatocytes, primary spermatocytes and spermatogonia. The tubules have two types of cells—spermatogenic cells which are sperm-forming cells and Sertoli cells which support spermatogenesis. The tubules converge to form the **rete testis**, from which arise vasa efferentia which form the epididymis.

Between the seminiferous tubules are special cells called **Leydig cells** or interstitial cells where testosterone and other androgens are produced.

2. Functions

The main function of the testes is to produce spermatozoa, which are essential for fertilization and hence reproduction.

Testes are the body's main source of the male hormone, testosterone. This hormone controls the development of the reproductive organs and other male characteristics, such as body and facial hair, deep voice, wide shoulders, etc.

3. Spermatozoa

A mature male germ cell develops in the seminiferous tubules of the testes by the process of spermatogenesis (spermatogonia → spermatocytes → spermatids → spermatozoa). It is about 50 μm long and has a head, a neck, a body and a tail that helps in propulsion. Spermatozoa are the generative component of the semen.

The head is oval and contains a nucleus of dense genetic material (23 chromosomes). The neck connects the head to the body. The neck is short and weak. The body has rings of fibrils covered with a sheath. The tail is made of protein fibers that contract on alternative sides. The fibrillary end of the tail has a ciliary characteristic, which causes wavelike movement which drives the sperm through the seminal fluid.

During each ejaculation, a few milliliters of semen is discharged. One hundred thousand spermatozoa are present in one cu mm of semen. Hence trillions of spermatozoa get discharged with each ejaculation. They remain alive for one to two months, but in the female genital tract they can survive for 24 to 72 hours only. Fertilization does not take place if the sperm count is less than 20 million per cc.

4. Undescended Testicles

Gonadal development occurs during the first 3 weeks of embryologic development. By twenty-eight weeks, the processus vaginalis, an out-pouching of the abdominal peritoneum, herniates through the abdominal wall and descends in the inguinal canal. The testes then descend through the inguinal canal into the scrotum following the processus vaginalis. Anomalies of the genital organs are the result of an abnormality at some state of embryologic development.

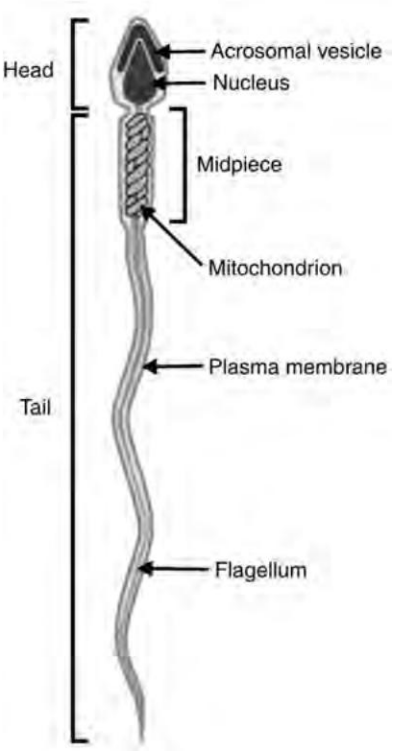


Fig. 16.19 *Spermatozoa*

The most common anomaly in the male genital tract is **cryptorchidism**. Many factors, both hormonal and mechanical, can result in undescended testes. Subsequent infertility, repeated injuries and testicular tumor formation are the most common problems related to cryptorchid testes.

Premature and low-birth-weight babies are at increased risk. A premature baby is at increased risk because the migration of the testicles hasn't had time to occur *in utero* (in the womb).

5. Ectopic Testis

Undescended testes may be truly cryptorchid or ectopic. Cryptorchid testes may be in an abdominal, inguinal or suprascrotal position. Ectopic testes can assume any position outside the inguinal canal.

There are usually no symptoms. In most cases of undescended testicles, only one testicle (testis) is absent. The scrotum is empty on the affected side. Sometimes, the scrotum is empty on both sides. The condition is painless. Urination is not affected. Adult males with an undescended testicle may have problems with infertility.

Virtually, all testes that eventually descend will do so by six months of age. Therefore, children with undescended testes after six to eight months of age should be considered for surgical correction. HCG stimulation therapy is usually

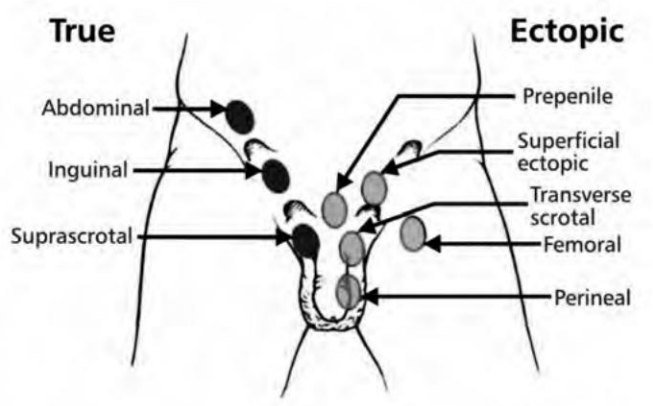


Fig. 16.20 *Cryptorchidism*

reserved for bilateral undescended testes. Even though it may not result in complete descent, subsequent orchidopexy is often technically easier after hormonal manipulation. Laparoscopy is both a diagnostic and therapeutic tool, being utilized more often, especially in cases of nonpalpable testes. Surgery at an appropriate time may prevent irreversible damage to the testicles. This damage can cause infertility. Bringing the testicle into the scrotum maximizes sperm production and allows examination for early detection of testicular cancer.

Sometimes a condition called **retractile testes** will develop. In this condition, the health-care provider can sometimes locate the testicles and sometimes not. This occurs because of the small size of the testicles before puberty and strong muscle reflex (cremasteric reflex) that retracts the testicles. In this instance, the testicles descend and settle in the scrotum at puberty. This is considered a normal phenomenon. Surgical correction is not needed.

16.4.2 Epididymis and Vas Deferens

The sperms which are formed are stored in the epididymis.

The seminiferous tubules converge to form the **rete testis**, from which arise vasa efferentia which form the epididymis

The epididymis can be divided into three main regions:

- The **head** receives spermatozoa via the efferent ducts of the testis. Histologically, it consists of a thin myoepithelium. The concentration of the sperm here is dilute.
- The **body** is the narrow mid portion.
- The **tail** is the smaller inferior portion and has a thicker myoepithelium than the head region, as it is involved in absorbing fluid to make the sperm more concentrated.

Distally, the tail continues as the ductus (vas) deferens. The vas deferens enters the pelvic part of the abdomen to enter into the prostatic part of the urethra where it is joined by the ejaculatory duct. Secretions from the prostate, seminal vesicle and bulbo-urethral glands empty here. They constitute the major portion of the semen.

16.4.3 Spermatic Cord

It is a cordlike supporting structure that ascends from the scrotum. It consists of the vas deferens (through which sperms pass in the process of ejaculation) and its accompanying arteries (testicular artery, deferential artery, cremasteric artery), nerves (nerve to cremaster, sympathetic nerves), pampiniform plexus, lymphatics and remains of *processus vaginalis*.

The spermatic cord is covered by three layers of tissue, viz., external spermatic fascia, cremasteric muscle with fascia and internal spermatic fascia.

The cord extends from the testes and passes through the inguinal canal up to the inguinal rings (openings at the level of the bladder) in the *fascia transversalis* (the connective-tissue sheath of abdominal wall muscles).

Applied Anatomy

The spermatic cord is sensitive to torsion, in which the testicle rotates within its sac and kinks off its own blood supply. Testicular torsion may result in irreversible damage to the testicle within hours.

The contents of the abdominal cavity may protrude into the spermatic cord, producing an indirect inguinal hernia.

16.4.4 Seminal Vesicles

The seminal vesicles are secondary sex organs. They are convoluted pouchlike structures and lie on the posterior aspect of the bladder and anterior to the rectum. Secretions of seminal vesicles are emptied into the ampulla of vas deferens. The seminal vesicle of both the sides joins to form the common ejaculatory duct, which forms the internal urethra within the prostate.

They secrete an alkaline, viscous fluid which contains fructose, prostaglandins and clotting proteins (different from those of blood). The alkaline nature of the seminal fluid neutralizes the acidic environment of the male urethra and female reproductive tract so that sperms are not inactivated or destroyed.

Prostatic ducts and bulbo-urethral glands open into the urethra.

The urethra passes through the penis and opens up exteriorly.

For details, refer the chapter on excretory system.

16.4.5 Prostate Gland

The prostate is a compound tubulo-alveolar exocrine gland of the male reproductive system.

It lies in the pelvic cavity behind the pubic symphysis and in front of the rectum, and is inferior to the urinary bladder surrounding the first part (prostatic part) of the urethra. The gland slowly increases in size from birth to puberty. Then the

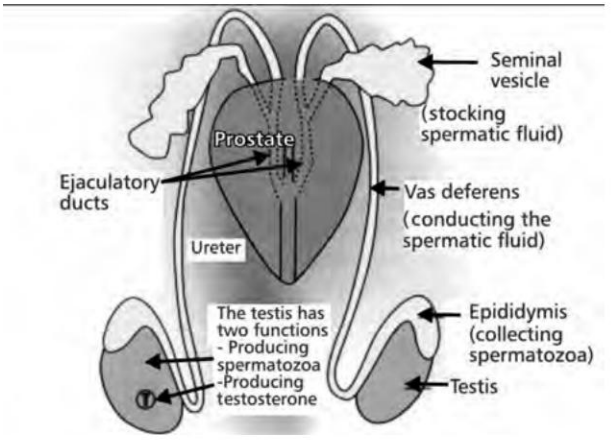


Fig. 16.21 *Prostate gland*

growth is fast up to the age of thirty, after which it is stable till 45, after which it again enlarges.

The main function of the prostate is to store and secrete a fluid, milky white in appearance that usually constitutes 25–30% of the volume of the semen, along with spermatozoa and seminal vesicle fluid. The prostatic fluid enters the prostatic urethra through many prostatic ducts.

This fluid is slightly acidic in nature, and contains citric acid, which is used by the sperm for ATP production. It also contains many proteolytic enzymes, e.g., Prostate Specific Antigen (PSA), lysozymes, etc., which break down the clotting proteins from the seminal fluid, seminalplasmin, which acts as an antibiotic and destroys bacteria and acid phosphates, whose function is not known.

Estimation of PSA level is important in diagnosing prostatic cancer. Prostate fluid helps prolonging the life span of spermatozoa in the vaginal tract.

16.4.6 Bulbo-urethral Gland

A bulbo-urethral gland, also called a **Cowper's gland**, named after the anatomist William Cowper, is one of two small exocrine glands, each approximately the size of a pea. They are homologous to Bartholin's glands in females. Bulbo-urethral glands are located posterior and lateral to the membranous portion of the urethra at the base of the penis, within the deep muscles of the perineum.

It has several lobules. Each lobule consists of a number of acini, lined by columnar epithelial cells. Ducts from each lobule join to form one duct, which opens into the spongy urethra. The glands gradually diminish in size with advancing age.

During sexual arousal, each gland produces a clear, viscous secretion. This fluid helps to lubricate the urethra for spermatozoa to pass through. It neutralizes the acid from the urine in urethra and helps flush out any residual urine or foreign matter. Mucus is also secreted by these glands, which also helps the process of lubrication. The Cowper's gland also produces some amount of prostate specific antigen and Cowper's tumors may increase PSA level.

16.4.7 Penis

The penis is the male copulatory organ and contains the urethra. It is the common passage for ejaculation of semen and excretion of urine.

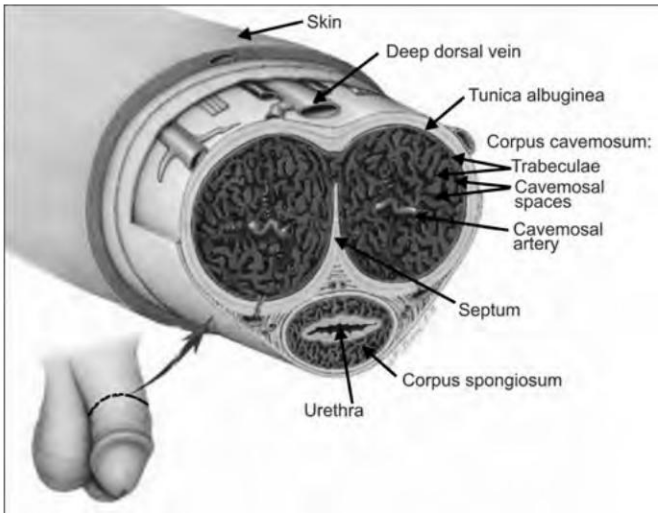


Fig. 16.22 *Penis and cross section at shaft*

Structure

It consists of the root, body and glans penis. The root is the attached portion and consists of the bulb and the crura. The tip is expanded into a triangular structure called the glans penis, above which the skin is folded upon itself to form a movable layer called the **prepuce**.

It consists of three cylindrical bodies of erectile (cavernous) tissue and involuntary muscle. Two of these are **corpora cavernosa** which lie in the dorsal part and form two lateral columns. The third is **corpus spongiosum** which contains the urethra. It is ventral to the corpora cavernosa. Each cavernous body is covered by a sheath of tunica albuginea consisting of collagen and elastic fibers. All the three bodies are bound by an elastic areolar tissue called **fascia penis**. Hair are absent on the penis except at the root.

Arterial Supply Deep, dorsal and bulbar arteries of the penis which are branches from the internal pudendal arteries.

Venous Drainage Veins drain into the internal pudendal and internal iliac veins.

Nerve Supply Nerve supply is by autonomic and somatic nerves. Parasympathetic stimulation causes arteriolar dilatation and venoconstriction which increases blood flow into the penis and obstructs outflow. This leads to filling of the spongy

erectile tissue with blood. So the penis gets engorged and erect. This is necessary for coitus to occur.

16.5 PHYSIOLOGY OF MALE REPRODUCTIVE SYSTEM

16.5.1 Spermatogenesis

Spermatogenesis occurs in all the seminiferous tubules during active sexual life, as a result of stimulation by anterior pituitary gonadotropic hormones. Normally, it begins at the age of 13 years.

It is the process by which spermatozoa are developed from the primitive germ cells called **spermatogonia**, which contain diploid number of chromosomes.

The entire process can be described in four stages.

1. Stages of Spermatogenesis

- Stage of proliferation
- Stage of growth
- Stage of maturation
- Stage of transformation

(a) Stage of Proliferation Larger spermatogonia are found near the basement membrane of the seminiferous tubule. Each has a diploid number of chromosomes (23 pairs). One member of each pair is from maternal origin and the other from paternal origin.

The spermatogonia divide by ordinary mitosis without change in chromosomal number.

Finally, the spermatogonia enter the stage of growth as the primary spermatocytes.

(b) Stage of Growth The primary spermatocyte grows into a larger cell with no other change.

(c) Stage of Maturation Each primary spermatocyte undergoes meiotic division, which occurs in two stages:

In the first stage, the cell divides and two cells (secondary spermatocytes) are formed which receive only half the number of chromosomes.

In the second stage, two spermatids are formed from each secondary spermatocyte. So there are four spermatids formed from one primary spermatocyte.

During the entire process, cytoplasmic separation does not take place and the cells remain in contact through the cytoplasm.

(d) Stage of Transformation The final development takes place and spermatids get transformed into spermatozoa. Each spermatid becomes a single sperm cell.

The entire period of spermatogenesis takes about 64 days.

Many factors regulate spermatogenesis of which Sertoli cells and hormones are the main ones.

2. Factors Affecting Spermatogenesis

(a) Role of Sertoli Cells Spermatogonia migrate centrally amongst the Sertoli cells. The Sertoli cells are arranged quite close to each other. These Sertoli cells nurture and provide nutrition to the developing sperms.

The Sertoli cells secrete estrogen which is essential for spermatogenesis.

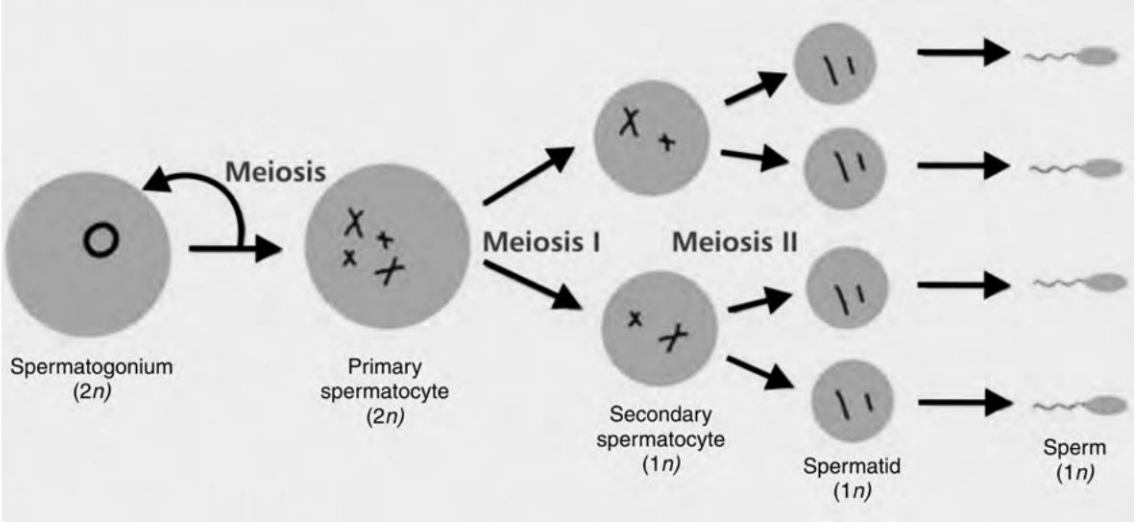


Fig. 16.23 *Stages of spermatogenesis*

Hormone-binding proteins secreted by these cells bind with testosterone and estrogen. They are then guided into the seminiferous tubules. These hormones are now available for the maturation of sperms.

(b) Role of Hormones Spermatogenesis is controlled and helped by many hormones. They are the following:

- Testosterone helps the growth and division of germinal cells and is also required for the formation of secondary spermatocyte from primary spermatocyte.
- Luteinizing hormone stimulates the Leydig cells to secrete testosterone.
- Follicle-stimulating hormone stimulates the Sertoli cells.
- Sertoli cells secrete estrogen which is helpful in spermatogenesis.
- Growth hormone stimulates division of spermatogonia. It is seen that in pituitary dwarfs, spermatogenesis is severely affected.

(c) Role of Other Factors Besides these hormones, there are certain other factors which control spermatogenesis.

- Successful spermatogenesis occurs at a temperature 3°C below the body temperature. The testes lie in the scrotum which is outside the abdomen, where the temperature is low as compared to intra-abdominal temperature. Increase in temperature prevents spermatogenesis.

  In undescended testes, the testes are in the abdomen where the temperature is higher and hence spermatogenesis is prevented because of degeneration of seminiferous tubules.
- Degeneration of seminiferous tubules occurs in certain infectious diseases, especially mumps and hence spermatogenesis does not occur.

3. Control of Spermatogenesis

1. The follicle-stimulating hormone of anterior pituitary stimulates spermatogenesis at the time of puberty.
2. A 3°C lower temperature in the scrotum helps in spermatogenesis. A hot bath at 45°C for half an hour leads to sterility.
3. Adequate supply of nutrients (carbohydrates, proteins, fats, vitamins—chiefly A, B, E, and ascorbic acid) is essential for spermatogenesis.

   Starvation hampers the process of spermatogenesis.
4. Experimental evidence has suggested that thyroid hormone, growth hormone, estrogen and sex hormones from adrenal cortex help in spermatogenesis.
5. X-ray irradiation and alcoholism decrease spermatogenesis.

4. Storage of Sperms

Storage of sperm occurs in

- Epididymis (small quantity)
- Vas deferens and ampulla (large extent)

Mature sperms are drained as follows:

Maturation of sperm occurs in the epididymis.

After ejaculation, the sperms become motile and they are capable of fertilizing the ovum. This process of maturation takes place with the help of hormones, which are present in the nutrient fluid secreted by the sertoli cells and epithelium of epididymis.

From epididymis, the mature sperms are emptied into the vas deferens. They go into the ejaculatory ducts and mix with the semen.

Normal sperms tend to travel in a straight line, rather than with a circuitous movement.

After entry into the vagina, sperms take 45 minutes to pass from the opening of the cervix to the end of the Fallopian tube.

If an ovum is present in the Fallopian tube, the sperm fertilizes it. Otherwise, the sperm dies, degenerates and disappears.

Sperms survive for 24–72 hours and can survive in slightly alkaline medium. They get depressed in slightly acidic medium and get destroyed in severe acidic medium.

5. Semen

Semen is the fluid ejaculated after a male sexual act.

(a) Contents

1. Sperms—10%
2. Fluid from seminal vesicle—60%
3. Prostatic fluid—30%
4. Small amount of fluid from bulbo-urethral glands

The pH of semen is 7.5.

The specific gravity of semen is 1.028,

The volume of semen, that is normally ejaculated, is 2.5 to 3.5 mL.

(b) Appearance Semen is milky due to prostatic fluid and is mucoid due to seminal fluid.

Fibrinogen is present in the seminal fluid which helps in fibrinogenesis after ejaculation, and this weak coagulum is important for holding the semen for some time in the cervix.

But after 15 to 30 minutes there is fibrinolysis.

(c) Life Span

1. In the genital ducts, they survive for many weeks.
2. After ejaculation, the sperms survive for 24 to 72 hours.
3. At 100°C temperature, they survive for 4 years.

(d) Normal Sperm Count The normal sperm count is 100 to 150 million / mL of semen. The average count is about 400 million/mL after ejaculation.

In case of sterility the count is less than 20 million/mL.

(e) Capacitation of Sperm After ejaculation, the sperm, though mature, is still inhibited by inhibitory factors from genital duct epithelia.

When the sperm comes in the female genital tract, multiple changes take place in the sperm. This sperm gets activated, which now is ready to take part in the process of fertilization of the ovum. This is known as capacitation. It occurs for 1–10 hours. The events which take place are as follows:

The uterine and Fallopian tube fluid wash the inhibitory factors.

The floating vesicle containing cholesterol from seminiferous tubules, which is released, allows cholesterol deposition around the acrosomic capsule membrane. So, the release of enzyme from the acrosomic capsule is prevented.

But in the vagina, the cholesterol covering is lost. The enzyme gets released, which facilitates fertilization.

Now, the membrane of the tail piece, which is called flagellum, becomes more permeable to calcium ions and hence the movement of the tail is increased. The calcium ions also cause intracellular changes in the acrosomic capsule and there is more release of enzymes which facilitate fertilization.

16.5.2 Physiology of Coitus

Coitus is a physical, biological act which requires the introduction of sperms from the penis into the vagina. There is erection of penis, ejaculation of semen and orgasm in the male and female.

Erection is the most prominent manifestation of sexual life. It is necessary for coitus and delivery of sperms into the vagina.

Erection is a reflex phenomenon which occurs in a man following the stimulation of the glans penis, or from visual cues or emotions or psychological stimulation. Impulses go via afferent nerves to the centers in the lumbosacral region of the spinal cord and impulses through the efferent path, i.e. the parasympathetic fibers cause arterial dilatation, which cause the muscles and blood vessels of the corpora cavernosa to relax. So the blood vessels of the corpora cavernosa open up, and blood rushes in through the cavernosus arteries to fill them. The blood then gets trapped under high pressure creating an erection. As these erectile bodies are surrounded by a strong fibrous coat, the penis becomes rigid, elongated and increases in girth. This compresses venous outflow so that while inflow increases, outflow does not. At the same time, parasympathetic nerves stimulate the bulbo-urethral glands to produce a mucoid-like substance to lubricate the urethra.

The tunica albuginea (the membrane surrounding the corpora cavernosa) helps trap the blood in the corpora cavernosa, thereby sustaining erection. Erection is reversed when muscles in the penis contract, stopping the inflow of blood and opening outflow channels.

Ejaculation is the process of emission of semen from the urethra into the vagina.

When there is friction between the glans penis and the vagina during the sexual act, impulses pass to the centers in the lumbosacral region. The centers then send impulses via the sympathetic fibers to the smooth muscles of the walls of the vas deferens and genital ducts which contract and push sperm into the upper part of the urethra. At the same time, the seminal vesicles and prostate gland contract and seminal fluid is released into the urethra.

Due to contractions of the bulbo-cavernous and urethral muscles (which are due to reflex activity of the somatic motor fibers of the spinal cord), the semen (sperm plus seminal fluid) is expelled from the urethra into the vagina.

The passage of semen from the upper part of the urethra back into the bladder is normally prevented by sympathetic contraction of the urethral sphincter.

An **orgasm** is the peak phase of the sexual response cycle, characterized by an intense sensation of pleasure experienced by both males and females. Orgasm is controlled by the involuntary, or autonomic, system, and is accompanied by quick cycles of muscle contraction in the lower pelvic muscles, which surround the primary sexual organs and the anus in both males and females.

Physiological changes also occur in other parts of the body. There is rise in blood pressure, increase in heart rate, flushing of the face and sweating. Endocrine glands like adrenal cortex with medulla, anterior pituitary and thyroid glands are also stimulated during intercourse.

Erectile dysfunction is failure to achieve erection or ejaculation or both or inability to hold the erection long enough for sexual intercourse. It is also called impotency.

It could be due to failure to initiate erection which could be due to psychogenic, neurogenic or endocrinal causes. It could also be due to failure to fill or failure to store adequate blood volume within the lacunar network. Other causes could be physical abnormalities of penis, penile surgery, testosterone deficiency, etc.

In older people it could be due to diabetes, atherosclerosis, or certain drugs like thiazides, beta blockers, etc.

16.6 DISEASES OF MALE SEX ORGANS

1. Epididymorchitis

This is the inflammation of the testes and epididymis. It could be nonspecific, due to spread of infection from the urethra following prostate operation or prostatitis. It could be due to infection or injury or sometimes due to gonorrhea following unsafe sexual intercourse.

2, Orchitis (Infection of Testes)

This could be due to mumps, a virus infection which spreads from parotids. Usually it is unilateral but rarely bilateral which, sometimes, could lead to sterility.

3. Prostatic Hypertrophy

This is seen in older people, usually after the age of 60. There is hyperplasia of the gland which surrounds the urethra causing its compression and hence there is obstruction in flow of urine. There is hesitancy, increased frequency, difficulty in voiding, nocturia or overflow incontinence. Alcohol or certain drugs, such as tranquilizers, can lead to retention of urine. The cause of enlargement is not clear but could be due to acceleration in the aging process associated with decrease in androgen secretion, leading to change in androgen–estrogen balance.

4. Prostate Carcinoma

It is age related and is a common cause of death in older males. The cause is not known. Some postulate it to be due to some virus. Some think it to be due to imbalance in androgen–oestrogen balance. Local tissue spread is followed by lymph spread to abdominal and pelvic lymph nodes. Spread through blood is mainly to bones of lumbar vertebrae.

5. Hydrocele

Accumulation of serous fluid in the tunica vaginalis leads to swelling of the scrotum. It may be acute or chronic, congenital or secondary.

6. Varicocele

Occasionally, the veins in the scrotum get congested and tortuous giving the appearance and feel of a bag of worms. It could be associated with hydrocele. The cause is not clear.

7. Testicular Cancer

Testicular cancer is most common among men aged 15–40 years. It has three peaks—infancy through the age of four as teratomas and yolk-sac tumors, ages 25–40 years as post-pubertal seminomas and nonseminomas, and from age 60 as spermatocytic seminomas. A major risk factor for the development of testicular cancer is cryptorchidism.

More than 95% of tumors arise from spermatogenic cells within the seminiferous tubules. A testicular mass can often be palpated. Because testicular cancer is curable when detected early, regular testicular self-examinations can help identify growths early when the chance for successful treatment is the highest.

Symptoms include a lump or enlargement in either testicle, a feeling of heaviness in the scrotum, a dull ache in the abdomen or groin, a sudden collection of fluid in the scrotum or pain or discomfort in the testicle or the scrotum.

REVIEW QUESTIONS

1. Describe the female reproductive system with functions.
2. Describe the supports of the uterus.
3. Describe the anatomy of the fallopian tubes.
4. Explain the position, structure and functions of the ovary with a neat diagram.
5. Describe the menstrual cycle.
6. Describe the changes in the cervix and vagina during the menstrual cycle.
7. Describe the development of mammary glands and their structure in detail.
8. Explain the various methods of fertility control.
9. Describe the physiological changes during pregnancy.
10. Describe the male reproductive system.
11. Describe the stages of spermatogenesis and the factors affecting it. How is it controlled?
12. Discuss the physiology of coitus.
13. Describe in brief the various disorders of male and female reproductive organs.
14. Write short notes on:
    a. Prostate gland
    b. Seminal vesicle
    c. Semen
    d. Oogenesis
    e. Implantation of embryo
    f. Structure of testis
    g. Erectile dysfunction
    h. Ovarian cycle
    i. Uterine cycle
    j. STD (Sexually Transmitted Disease)
    k. Structure of penis

The McGraw·Hill Companies

Chapter

17 Defense System

- **NON-SPECIFIC DEFENSE MECHANISM**
  - Inflammation ..... Acute inflammation
    ..... Chronic inflammation
- **SPECIFIC DEFENSE MECHANISM**
  - Immunity ..... Humoral immunity
    ..... Cell-mediated immunity
    ..... Antibodies
- **RETICULO-ENDOTHELIAL SYSTEM**
- **DISORDERS**
  ..... Hypersensitivity or allergy
  ..... Auto-immune disease
  ..... Acquired immune deficiency syndrome (AIDS)

Introduction

The human body is constantly attacked by bacteria, viruses, parasites, cancer cells, solar radiation and pollution. Mental stress is another challenge for maintaining a healthy body. The body, hence, has developed a defense system for its protection.

The body has two layers of defense systems:

- Nonspecific defense mechanism
- Specific defense mechanism

17.1 NON-SPECIFIC DEFENSE MECHANISM

The **intact skin and mucous membranes** provide a mechanical barrier to pathogens and toxins. They also secrete chemicals that either inhibit or destroy bacterial growth. Cilia along with mucus trap and remove organisms.

There are **certain antimicrobial substances** in the body which prevent microbial growth or destroy the microbes.

Normal flora of the gastrointestinal tract suppresses growth of virulent organisms. The stomach contains **hydrochloric acid** in the gastric juice by which many microbes are killed and then digested by the proteolytic enzymes. **Absorption in the small intestine** is so rapid that any residual microbes cannot survive here. Also, the intestines are anaerobic so aerobes cannot multiply here. The **large intestinal wall** is coated with a protective mucus layer which prevents the contents in coming in contact with the cells lining the large intestine.

Hairs in the nose act as filters. Antibodies present in nasal secretions inactivate certain microbes.

Sweat glands secrete a mixture of salt and fatty acids which inhibits many microbes.

Foreign materials and microbes are washed out by the **tears** from the eyes.

The **Epiglottis** does the important function of preventing dust and microbes from entering the trachea.

Saliva washes out the foreign material stuck in between the teeth. Continuous flow of saliva through the mouth flushes microbes into the stomach.

Acidic pH in the vagina inhibits growth of bacteria and fungi. The acidic urine prevents or inhibits bacterial growth.

Interferons are substances produced by T-lymphocytes and the cells invaded by viruses, which prevent spread of viruses and their multiplication.

The **complement system** consists of a number of small proteins found in tissues and blood, synthesized by the liver, and is normally inactive. It is activated by immune complexes—antigen–antibody complex. Cytokines are liberated. The complement attracts phagocytes to an area of infection. It kills the microbe by binding to the membrane and destroys it. It stimulates phagocytosis by binding to the bacterial cell wall. Phagocytosis is a form of endocytosis.

Neutrophils and macrophages are attracted by chemical attractants towards the site of inflammation or a bacteria or virus. The phagocytic cell changes shape and sends projections, called pseudopodia, that make contact with the particle. A receptor–ligand interaction occurs between these two particles and the pseudopodia surround the infected particle, grasp it and ingest it. Hence any foreign material is bound, grasped and digested by the phagocytic cell.

17.1.1 Inflammation

Inflammation is a nonspecific physiological defense mechanism which protects and prevents tissue damage from foreign invasion. Reaction takes place in tissue cells, blood cells and blood vessels. The purpose is to remove the injurious stimuli and initiate healing process. A sequence of changes takes place.

Inflammation can be classified as acute or chronic. Acute inflammation involves vascular system, the immune system and various cells within the injured tissue. Prolonged inflammation is chronic inflammation involving proliferative changes with simultaneous destruction and healing of the tissue.

Causes

- Infection by pathogens—bacteria, viruses, protozoa, fungi
- Chemical irritants
- Physical injury or agents like heat, cold
- Toxins
- Burns, ionizing radiation
- Immune reactions due to hypersensitivity
- Foreign bodies

1. Acute Inflammation

Acute inflammation is a short-term process—days to weeks. There are five cardinal signs:

- Pain—dolor
- Redness—rubor
- Heat—calor
- Swelling—tumor
- Loss of function—function laesa

Heat and redness are due to increased blood flow. Pain is due to release of chemical substances. Swelling is due to accumulation of fluid. Loss of function is due to a mixture of many causes, one of them is a neurological reflex in response to pain. These signs are seen when the inflammation occurs

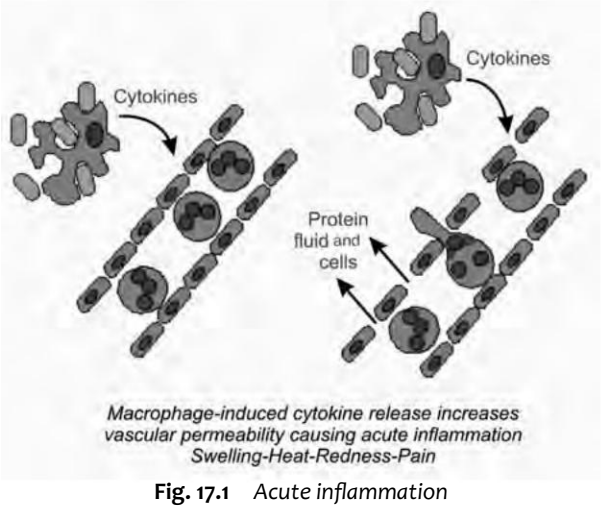


Fig. 17.1 *Acute inflammation*

on the surface of the body. All these signs may not be present in case of inflammation of internal organs.

The process of acute inflammation occurs in a series of stages—increase in blood flow, formation of tissue fluid and migration of leucocytes, mainly neutrophils. It is initiated by cells already present in the tissues.

(a) Increase in Blood Flow Whenever there is damage to a tissue, there is release of chemical mediators (serotonin, histamine, kinins, and prostaglandins), which are responsible for vascular changes in the form of vasodilatation of arterioles and capillaries, leading to increased blood flow. Vasodilation and increased blood flow causes redness and heat.

Vasodilation leads to stasis and along with chemical mediators causes increase in capillary permeability. This results in exudation of plasma proteins and fluid into the tissue causing edema which is seen as swelling. Leakage of plasma proteins causes decrease in osmotic pressure of the blood and hence fluid moves from blood into the tissues.

The slowing of blood flow causes the white blood cells, mainly neutrophils, to come close to the vessel wall and adhere to the endothelium and migrate out into the tissue. These neutrophils, due to chemotaxis (by substances released from bacteria and damage tissue), are attracted to the site of injury. The main function of the neutrophils is phagocytosis of the antigens or the foreign material. They engulf the biological material like microbes and damaged cells and are then digested by the enzymes. Nonbiological materials like chemicals and dust are not digested. If the material is in large amount or if digestion is resisted then the phagocytes disintegrate and die and release material that gets fibrosed. Phagocytic activity is promoted by raised temperature and protective proteins like antibodies. Toxins are neutralized.

(b) Exudate Fluid collects due to increased capillary permeability, which is colored and contains leucocytes, fibrinogen, erythrocytes and a high concentration of proteins. Monocytes are converted into macrophages, histiocytes and giant cells. Plasma dilutes toxins. Immune bodies modify the course of inflammation. Tissue repair is promoted by proteins. Swelling is due to exudate and it presses on the nerve endings causing pain.

Endogenous pyrogens are released from macrophages which causes rise in body temperature. Increase in temperature inhibits growth and division of microbes and phagocytic activity is promoted.

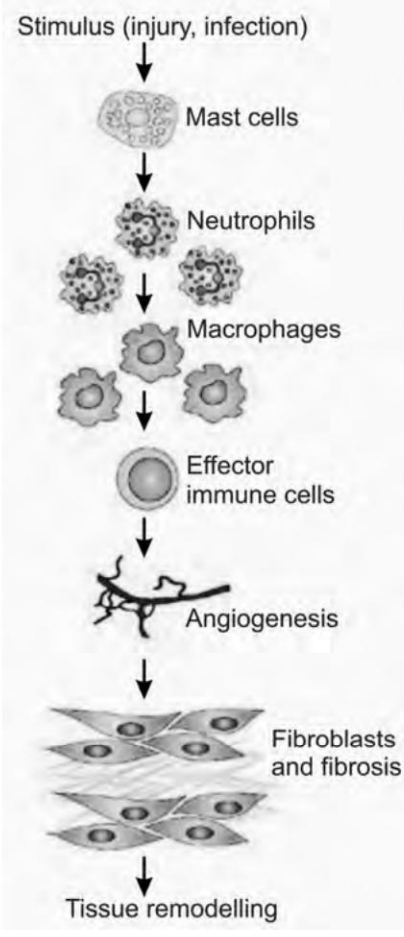


Fig. 17.2 *Stages of acute inflammation*

Fibrinogen is converted to fibrin by the action of thromboplastin, released from the damaged cells. This fibrin network can prevent spread of infection by forming a wall around the inflamed area, or it can join the edges of the area to promote healing. Sometimes certain microbes secrete toxins which dissolve the fibrin, thus making the tissue more vulnerable to the spread of infection.

Inflammation can terminate depending on the resistance of the person and on the virulence of the microbes. If the person's resistance is good and the virulence of the infecting agent is mild then the exudate, cell debris and phagocytes are removed by the lymph vessels and returned to blood. But, if resistance is

low and/or the virulence of the causative agent is high, the dead and damaged tissue undergoes necrosis, softening and liquefaction. This is commonly seen with infection by *Staphylococcus aureus* and *Streptococcus pyogenes*. This phenomenon is called **suppuration** and the material is called pus.

Pus is a collection of dead cells, phagocytes, fibrin, cell debris, exudate and living and dead cells. Fibrinogen is converted to fibrin by coagulase produced by staphylococcus and the pus gets localized. Streptolysins are produced by streptococcus which promotes breakdown of tissue. Thus, infection spreads. A collection of pus in a tissue, organ or a confined place is called an **abscess**. An abscess, which is superficial, ruptures through the skin and pus is discharged. If the damage is not extensive, healing takes place with treatment. If the abscess is deep, either it ruptures and heals or it develops into chronicity and keeps on discharging continuously through a channel called sinus. Sometimes the pus is walled off by fibrous tissue and gets calcified but organisms are still present and can again cause recurrence of infection later on when body resistance decreases. Occasionally, the healing is by fibrosis and if it occurs in an organ, it could cause narrowing of lumen or obstruction, e.g., in the intestine or esophagus.

(c) Resolution of Inflammation Resolution occurs when the cause is detected and treated. Resolution occurs by different mechanisms in different tissues. Harmful substances are phagocytosed and removed. New cells originate. Parenchymal cells carry out the function of tissue repair, and reconstruction of the injured tissue takes place. Fibrin strands are broken down by fibrolytic enzymes. Fibrosis occurs and there is scar formation. Repair is complete and a scar remains.

The debris is removed by the lymphatic system.

2. Chronic Inflammation

Occasionally, if the acute inflammation does not resolve and if the injurious agent persists, it goes into chronicity. Live microbes are present at the site, especially in deep-seated infections, as in bone infections and deep-seated abscesses. It may last for many days, months or even years.

The inflammatory cells like lymphocytes, plasma cells and macrophages are present in the injured tissue. Fibroblasts are activated and there is formation of collagen and fibrosis. Macrophages are powerful defensive agents but they release toxins, which injure the body's own tissue also along with the invading agent. Hence, there is tissue destruction.

The root cause of chronic inflammation is an imbalanced immune system. The body's defense cannot clear the infection and the area gets walled off forming a granuloma. The best example is tuberculosis, where the organism is resistant to the defense mechanism and a granuloma forms.

Chronic inflammation can also occur due to allergic reaction following repeated exposure to chemicals, prolonged exposure to toxic agents and exposure to silica. Antigen–antibody reaction following exposure to chemicals, where the antigen is an altered protein, can also cause chronic inflammation.

Inorganic substances, like an undissolved stitch or cotton, can lead to chronicity of a wound.

Poor blood supply to the injured part can also cause chronic inflammation.

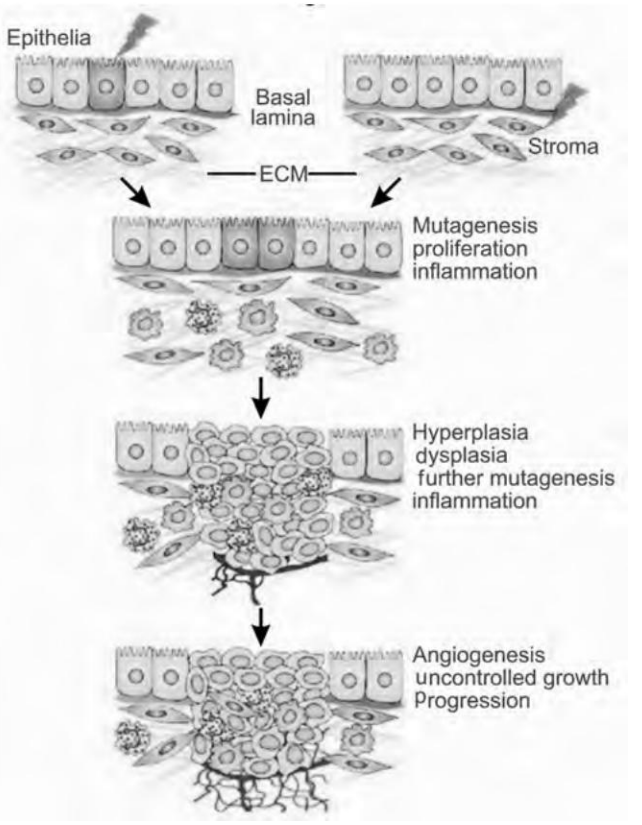


Fig. 17.3 *Carcinogenesis*

It has also been connected to diabetes, high blood pressure, obesity, cancer, atherosclerosis, depression and old age.

Outcome of Chronic Inflammation Cells which are destroyed cannot regenerate and there is attempt at repair by fibrosis. There is formation of granulation tissue. Here, surrounding tissue may get damaged.

There is angiogenesis—new vessel formation.

Necrosis and suppuration could resolve, when treated medically or surgically, with the formation of fibrous tissue and adhesions, e.g., stricture of the intestines.

An embolus or thrombus may cause an infarct and dysfunction of that part, e.g., brain dysfunction.

Contractures may develop; limb or joint movement may get affected.

Sometimes the chronic focus—lymph node—may burst out forming a discharging sinus. Pus from an internal organ could

find its way to the exterior (skin) and discharge the infected material leading to the formation of a fistula.

With early diagnosis, good treatment and better awareness, the percentage of chronicity is becoming less.

17.2 SPECIFIC DEFENSE MECHANISM

17.2.1 Immunity

Immunity is a biological process within the body that protects against pathogens and toxins, which can damage tissues and organs. It detects a wide variety of agents—bacteria, virus, parasites and toxins—and must distinguish them from the body's own tissue.

The nonspecific responses have already been discussed, of which inflammation is one of the first responses of the immune system to infection. They are present from birth and passed on from generation to generation. They vary from individual to individual.

The other type of immunity is **acquired immunity**. It is not present at birth. It is also called **specific immunity**. This immunity acts in response to a foreign substance entering the body.

Antigens are protein molecules found on the surface of the pathogens—virus, bacteria or toxins. The immune system consists of cells that have specific receptors on their surfaces which recognize and destroys the substances containing the antigens.

It has certain characteristics:

It has the ability to learn, remember and adapt. When first exposed to an antigen, immunity takes time to develop. It develops faster to a previously encountered antigen and subsequent responses to it are more effective.

The immune system normally does not attack its own body tissue. This is because there is a very good balance between the immune reaction and its suppression. But, sometimes, antibodies may be produced against the body's own tissue. This is called auto-immunization, as seen in myasthenia gravis, rheumatic fever, etc.

There are two types of acquired immunity—humoral and cell mediated. Lymphocytes are involved in both the types of immunity.

Lymphocytes may be T cells or B cells.

1. Humoral Immunity

Here, there is B-cell response. B cells are formed in the bone marrow. They have particular receptors on their surface where antigens can get fixed.

When the B cell encounters an antigen, the antigen attaches to a receptor stimulating the B cells. Some B cells change into memory cells and remember the specific antigen, while others change to plasma cells. Helper T-lymphocytes help in this process. Plasma cells produce antibodies which are specific to the antigen that resulted in its production. They produce only one type of antibody. This antibody production takes many days after exposure to the antigen for the first time. This is called primary immune response, which is slow to develop.

When the B cells encounter the same antigen again, they quickly recognize the antigen and begin to multiply rapidly and produce antibodies. This is secondary immune response and is very effective and quick.

2. Cell-mediated Immunity

Here, the T lymphocytes directly react with the foreign material. T lymphocytes act in different ways or there are different types of T cells.

They respond quickly when encountered with the same antigen again. These are **killer T cells** which kill the cells by making a hole in the cell membrane. Enzymes are pushed into the cell which disintegrates the cell.

Helper T cells help other immune cells and help the B cells to produce antibodies. They produce chemicals called cytokines, which promote cytotoxic T lymphocytes.

Suppressor T cells produce substances which prevent harmful responses to take place or help to end the immune response.

Cytotoxic T cells inactivate any cells carrying antigens. They attach to the cell and release toxins which are very effective. They destroy abnormal body cells and are seen in infected cells and cancer cells.

3. Antibodies

Antibodies are immunoglobulins produced on exposure to an antigen. They are highly specific, i.e., they are produced in response to a particular antigen. They protect the body by helping cells ingest antigens, by attacking the foreign substance directly, by inactivating toxic substances produced by bacteria and by activating the complement system. They are essential for fighting bacterial, viral and fungal infections.

Each antibody has two parts—one part is specialized to attach to a particular antigen only. The other part has five types—IgM, IgG, IgA, IgE and IgD.

From the immunity point of view, IgG and IgM are important. IgM is produced during primary response while IgG is produced during secondary response.

17.3 RETICULO-ENDOTHELIAL SYSTEM

The reticulo-endothelial system consists of phagocytic cells located in the different organs of the body. It is an essential component of the immune system. The organs, where it is found, are functionally interconnected. The cells are of two types—fixed and wandering cells. The fixed cells are the Kupffer cells of the liver, tissue histiocytes, the reticular cells in the spleen and lymph node and the microglial cells in CNS. The wandering cells are the monocytes, macrophages and abnormal foreign cells.

Phagocytic cells engulf substances like bacteria and viruses so that they cannot cause harm to the body. They manufacture plasma proteins and bile pigments. New RBCs and WBCs are formed. They play an important role in the formation of antibodies for body defense.

17.4 DISORDERS

1. Hypersensitivity or Allergy

An allergy is a hypersensitivity disorder. It occurs on exposure to normally harmless substances, commonly called allergens. Allergies are acquired reactions and are harmless. Allergens are usually in the form of dust, food, animal hairs and pollen. Common allergic reactions are eczema, hay fever, food allergies, reaction to insect bites and asthmatic attacks.

When there is exposure to an antigen for the first time, the person gets sensitized to it. On further exposure, reaction takes place and usually symptoms are mild which are in the form of sneezing, running nose, rashes and watering of the eyes. Occasionally, a severe reaction, called anaphylaxis, could occur which could be life-threatening.

There are four mechanisms of hypersensitivity.

(a) Type I: Immediate or Anaphylactic Hypersensitivity

There is excessive activation of certain white blood cells, called mast cells, and basophils by a type of antibody known as IgE. There is an extreme inflammatory response. IgE binds very specifically to receptors on the surface of mast cells and they remain circulating. When there is reintroduction of the same antigen, it interacts with IgE causing the cells to disintegrate and release histamine and other granular contents which leads leading to smooth muscle contraction, vasodilation, increased vascular permeability, broncoconstriction and edema. There is exudation of fluid and proteins into the tissues. This is followed by shock and may lead to death.

(b) Type II: Cytotoxic Hypersensitivity This involves antibody-mediated reactions. The antigen is located on the surface of the target cell. The antibody is IgG which is present in the blood. When it reacts with the antigen, the cell is phagocytosed and undergoes lysis. It may also activate the complement system. Normally, bacteria are eliminated in this way. But, sometimes, the antibodies may act on the body's own tissue causing an auto-immune response. This is seen in auto-immune hemolytic anemia. This mechanism causes other conditions like transfusion reactions and hemolytic disease of the newborn.

(c) Type III: Immune Complex Hypersensitivity This type of reaction involves a circulating antibody that reacts with a free antigen. These circulating immune complexes are deposited in the tissues. There is an acute inflammatory reaction. It activates a complement causing release of histamine and there is increased vascular permeability. There is increase in leucocytes and phagocytosis. The kidney is a common site of deposition for immune complexes, especially in the glomeruli, which are blocked and there is impairment of kidney function. Another example is sensitivity to penicillin, where the immune complexes are deposited in the tissues and there is joint pain, rashes and hematuria.

(d) Type IV: Delayed Hypersensitivity It is a cell-mediated response. It is seen in response to bacteria, viruses or fungi. Here, the reaction occurs very slowly. The hypersensitivity is mediated via T cells and macrophages. There is destruction of, both, specific and nonspecific microorganisms and the T lymphocytes could damage normal tissue also if their response is not controlled.

2. Auto-immune Disease

An immune response is against foreign material. But, if the immune response actually attacks its own cells there is an overactive immune response of the body resulting in auto-immune diseases.

The immune system mistakes some part of the body as a pathogen and attacks it. It may involve a particular tissue at different places or certain organs, e.g., Graves' disease, myasthenia gravis, Hashimoto's disease and rheumatoid arthritis.

3. Acquired Immune Deficiency Syndrome (AIDS)

Acquired immune deficiency syndrome is a disease caused by the human immunodeficiency virus. There is progressive reduction in the effectiveness of the immune system and the person becomes susceptible to opportunistic infections.

It is transmitted by direct contact of a mucus membrane or blood with a bodily fluid containing the virus—semen, blood, vaginal fluid and breast milk. Infection is spread by sexual intercourse, blood transfusion, substance exchange between

mother and child during pregnancy and use of contaminated needles.

Pathophysiology HIV is a retrovirus that primarily attacks organs of the immune system that have a protein receptor CD4 in their membrane including macrophages and dendritic cells. Once the virus has killed enough of these cells (the number becomes less 200 per microliter), the cellular immunity is lost.

The retrovirus produces an enzyme, **reverse transcriptase**, inside the host cell which transforms viral RNA into DNA. This incorporates into the host cell DNA. Now, new copies of the virus are produced which enter the blood and tissue fluid and infect other cells, which divide. Copies of the provirus are then integrated into the DNA of daughter cells, spreading the disease everywhere in the body.

REVIEW QUESTIONS

1. Define and classify allergy. Discuss the features of various types of allergy.
2. Write a note on the reticulo-endothelial system.
3. Discuss nonspecific defense system. Define inflammation. Describe the basic mechanism of inflammation. Write in detail about acute and chronic inflammation.
4. Categorize immunity. Describe each category.
5. Write short notes on:
   a. Complement system
   b. AIDS
   c. Inflammation and repair

The McGraw·Hill Companies

Chapter
18
Physiology of Aging

Introduction

People are living longer due to better living standards and advances in medical science. With advancing age, the anatomy and physiology of the body changes. Aging is a progressive physiological process. There is degeneration of tissues, organs and systems with decrease in function. This results in inability of the person to cope with physiological challenges. Many of these changes are involuntary and occur gradually while some changes take place over a short period.

Cell

Gene mutations or production of harmful substances leads to decrease in the vitality of the tissue. There is decrease in DNA, RNA and ATP. Nuclei become small and compact. The cell shows cavitation and decrease in metabolic activities. Granules in the cytoplasm become small and finally disappear.

Respiratory System

Lung and chest-wall compliance decrease as age advances. Total lung capacity, forced vital capacity and vital capacity are reduced while residual volume increases and functional residual capacity remains the same. Elastic tissue in the airways decreases and there is increased collapsibility of alveoli. Breathlessness occurs due to lack of oxygen.

Cardiovascular System

Arteries become atherosclerotic and thick. Medium-sized vessels become less elastic and compliance decreases. There is an increase in peripheral resistance and hypertension results. This results in left-ventricular strain and left-ventricular hypertrophy. There is decrease in the blood supply to the various organs resulting in decreased functioning of these organs.

Cardiac output reduces and there is decrease in the circulation time through the tissues. Cardiac conducting cells decrease in number, resulting in cardiac blocks, arrhythmias and ectopic beats.

Ischemic heart disease is common in older persons, especially in diabetics and smokers. Even without objective evidence of coronary heart disease, older people (nearly 60%) should be considered at increased cardiovascular risk.

Excretory System

Glomerular filtration rate decreases by 1% per year after the age of 20 years. This is due to progressive loss of renal cortical glomeruli. Due to decrease in cardiac output and atheromatous vascular disease, renal perfusion decreases. Nearly 50% of nephrons are lost after the age of 60 years.

Other factors which decrease renal function are diabetes, nephrotoxic drugs and ACE inhibitors. Prostate hypertrophy causes obstructive nephropathy. Dehydration due to any reason causes renal dysfunction very quickly in elders.

Endocrine and Metabolic

Basal metabolic rate falls by 1% every year after the age of 30. Decreased metabolic activity and reduction in muscle mass impairs thermoregulatory control.

Endocrine atrophy leads to metabolic instability. There is increased incidence of thyroid disorders, osteoporosis and nutritional disorders. Aged people also have diabetes (25%) and hence there is increased incidence of renal impairment, cardiovascular disease and retinopathy.

Vitality and strength of the body decreases and there is easy fatigability and lack of interest in activities.

Nervous System

Cerebrovascular disease is common in the elderly, secondary to diffuse atherosclerosis and hypertension. There is decrease in neuronal density by 30% by the age of 80 years. It occurs more in the frontal lobes.

Cognitive impairment occurs, common causes of which are dementia, Alzheimer's disease and Parkinsonism.

There is decrease in the blood supply to the brain. Hence memory, judgment and behavioral functions are altered. Memory loss is mainly for recent events. Many repeat the same event repeatedly. The ability to cope with life deteriorates.

Visual and hearing impairment are common and this can lead to difficulty in communication.

Autonomic neuropathy can lead to impaired response and hemodynamic instability. There is delayed gastric emptying and increased gastric aspiration.

Musculoskeletal System

Osteoporosis occurs especially in females, immobile persons and those who are on long-term steroids. Arthritis is common and leads to pain and reduced mobility. Bones lose calcium and can easily be fractured. These persons must be moved with caution. Bones and joints may be deformed. Prominent bony areas are susceptible to skin abrasions and pressure sores.

Body weight is reduced due to loss of tissue and the old get tired very easily. General weakness is common.

Nutrition and Digestive System

Appetite decreases. Digestion gets disturbed and absorption decreases. Diarrhea and/or constipation are common. More than 40% lose their teeth and may have to use dentures. Gums shrink and hence dentures may not be easily adjusted. Intake of food becomes less. Caloric needs are decreased. Production of alimentary juices is reduced.

Body temperature is reduced and susceptibility to cold decreases.

Pharmacology

Reduced total body water and loss of tissue leads to an altered volume of distribution of some drugs. There is reduction in plasma proteins resulting in decreased protein binding and increased free-drug availability. Reduced cardiac output results in delayed onset of intravenous anesthesia.

Integumentary System

Aging causes changes in the skin, hair, glands and nails.

With advancing age, skin and fat tissue become thinner and less elastic. The skin becomes more translucent and prone to injuries and infection. Healing is also slow and takes twice the time as taken in younger people. The skin is wrinkled and fragile and bruises easily. Dermis is less elastic and becomes less resilient. This becomes more pronounced in areas exposed to the sun, leading to decreased ability to maintain body temperature and the person feels colder. The ability to lose heat decreases also due to reduction in the blood supply to the dermis and reduction in sweat gland activity. Overexertion can cause dangerously high body temperature. Extreme temperatures of either heat or cold can produce harmful effects on the body.

There is reduction in surface contact between the epidermis and dermis resulting in reduced exchange of nutrients and metabolites between the two layers.

Loss of fat tissue behind the eyes gives the eyes a sunken appearance and the face seems more bony.

Oil glands produce less oil. There are fewer sweat glands. Sebaceous-gland activity declines and there is less production of sebum. This causes less perspiration leaving the skin dry, scaly and itchy.

Vascularity of nail bed decreases, resulting in dull, hard and thick nails with a slowed growth rate. Fingernails may become brittle or develop ridges. Toe nails develop a disk shape, grow more slowly and thicken.

Less vascularity and decreased circulation in the subcutaneous tissue decreases absorption of drugs.

Less melanin is produced and hence the hair color fades to grey or white. There is decreased protection from ultraviolet light leading to more susceptibility to sunburn and skin cancer. Selected melanocytes increase their production in areas exposed to the sun which results in brown spots on the skin.

As the number of macrophages and other cells of the immune system decreases to less than 50%, risk of infection increases and leads to skin damage.

REVIEW QUESTIONS

1. Discuss in detail the aging process.
2. Write short notes on the effects on each of the following with respect to the aging process:
   a. Cell
   b. Respiratory system
   c. Cardiovascular system
   d. Excretory system
   e. Endocrine system and metabolic process
   f. Nervous system
   g. Musculoskeletal system
   h. Digestive system
   i. Integumentary system
   j. Pharmacology

The McGraw·Hill Companies

Chapter 19

Health Education, Communicable Diseases and Family Planning

- **DISEASE**
  - **Types**
    - **Deficiency**
    - **Hereditary**
    - **Physiological**
    - **Pathological**
      - **Bacteria**
      - **Viruses**
      - **Protozoa**
      - **Fungi and moulds**
      - **Helminths**
      - **Spread of infection**
      - **Prevention of infection**
- **CERTAIN USEFUL TERMS**
- **COMMUNICABLE DISEASES**
  - **Water-borne diseases** ..... **Spread of disease, Preventive measures**
  - **Air-borne diseases** ..... **Spread of disease, Preventive measures**
  - **Arthropod-borne infection** ..... **Spread of disease, Control of arthropods**
  - **Rodents** ..... **Control of rodents**
- **MALARIA**
  - **Life cycle of the malarial parasite**
  - **Prevention of Malaria**
  - **Other diseases**
- **WORM INFESTATION**
- **SEXUALLY TRANSMITTED DISEASES**
- **FAMILY PLANNING**

Introduction

There is an old saying 'health is wealth'. It is also well said that "prevention is better than cure". Hence it is imperative to educate the society about health to promote health and prevent disease, premature death and disability.

Health education is closely related to medicine. It enhances the quality of life. Special attention is given to prevention of diseases, thus reducing the cost of medical treatment of a person, group, community and the nation.

In recent years living and working conditions have improved greatly. There is good social, physical and psychological environment, modern approaches are used for comforts of life and education at school, college and community levels has improved. Along with this progress, one must be aware of the effects of environment on the body. The body has to fight against the natural environment as well as various infections.

19.1 DISEASE

Disease is an abnormal functioning of various organs of the body associated with certain symptoms and signs. It can be caused by external factors like infections or may occur due to internal dysfunction like auto-immune reactions. Any condition that causes distress, pain, dysfunction or social problems is called a disease.

19.1.1 Types of Disease

There are four main types of disease—deficiency disease, hereditary disease, pathogenic disease and physiological disease. Disease can also be classified as communicable and noncommunicable.

Examples of **deficiency diseases** are malnutrition conditions like beri-beri (vitamin B_1 deficiency), scurvy (vitamin C deficiency), anemia (vitamin B_{12} / iron deficiency), etc. Excess of certain nutrients can lead to certain diseases, e.g., goiter (iodine deficiency).

Examples of **hereditary conditions** are cystic disease, muscular dystrophies; heart conditions, e.g., foramen ovale, etc.

Physiological conditions are due to physical agents like cold, radiation, heat, etc., and exposure to these agents can cause adverse effects. Mechanical agents like injury; pressure, etc., can also cause damage to the body.

Pathologic diseases are the most important and occur due to various infections, pathogens and chemical agents.

The body can be invaded by various agents like bacteria, virus, fungi, protozoa and worms. After invasion, these pathogens multiply in a part of the body or tissue causing tissue injury and progress to overt disease through a variety of cellular or toxic mechanisms. Most common infections are bacterial and viral. They both cause malaise, fever, chills and body ache. The difference between the two is that a virus does not respond to antibiotics.

Infections can be local like an abscess or generalized like septicemia. They can be exogenous, i.e., that which originates outside the body and endogenous, which occurs when the body's resistance is lowered.

Infectious agents can enter the body by inhalation, ingestion, sexual transmission, wound infection, insect bite or from mother to the fetus during pregnancy or birth.

When the pathogen invades, the body responds by forming antibodies or antitoxins. Antibodies give immunity. Antitoxins cause ill effects like malaise, rise in body temperature and weakness.

When the body's resistance is lowered, it increases the chances of endogenous infection. Lack of sleep, malnutrition, poor eating habits, trauma, prolonged exposure to cold, etc., can lower the body's resistance. Drug abuse, alcohol and tobacco consumption can also lower the body's resistance.

Hence, it is necessary to make the masses aware of food habits, bad habits (vices), proper health care and ways of preventing diseases.

1. Bacteria

Unicellular microorganisms present in plants, animals, fluids and in the atmosphere are called bacteria. Pathogenic bacteria cause disease. Some bacteria are useful, e.g., preparation of curds, and some help to break down dead organic matter. Some present in the guts help in vitamin B_{12} manufacturing:

Bacteria are classified according to their shapes.

Table 19.1 *Classification of bacteria*

Bacteria	*Shape*
Cocci	Round or oval-shaped
Bacilli	Rod-shaped
Spirochetes	Spiral-shaped
Vibrios	Comma-shaped
Spirilla	Wavy, curved, spiral-shaped
Actinomycetes	Branched
Mycoplasm	Interlacing filaments, without cell wall

Another way of classification is according to their staining reactions depending whether they are stained by gram stain or not.

Gram positive or Gram +ve—streptococci, staphylococci, enterococci, etc.

Gram negative or Gram –ve—gonococci, *E.coli*, salmonella, etc.

There is a third group called **acid fast bacilli** which have different staining characteristics, e.g., *Mycobacterium tuberculosis* and *Mycobacterium leprae*.

Properties of Bacteria Bacteria are prokaryocytes. Their DNA is not enclosed in the nucleus.

They are found everywhere—in the water, soil, on the skin and inside the body. They multiply very rapidly under favorable conditions and aggregate into colonies of millions of organisms in a space as small as a drop of water.

They consist of only one cell and lack chlorophyll.

Except for viruses, they are the smallest living organisms. Many are so small that a million of them if placed end to end would not measure more than five centimeters.

Bacteria need food for survival which they obtain from the surrounding medium in dissolved form.

All bacteria have a particular temperature range for survival. Most of them grow between 37°C and 38°C and die at 70°C. They become dormant in the cold environment and again grow when the environment becomes warm.

Bacterial growth is affected by pH. Most bacteria require a pH of 6.7 to 7.5.

They may or may not need oxygen to grow. Those that need oxygen are called **aerobic bacteria**, and those that do not require oxygen are called **anaerobic bacteria**.

They reproduce by fission or they multiply. They multiply very fast—up to millions and billions in a day and also die equally fast.

Some bacteria are useful and improve human life while others cause disease and still others have no overall effect on humans.

The best example of helpful bacteria is *E. coli* found in the digestive system which helps break down many types of food. Bacteria are also responsible for production of certain vitamins such as vitamin B and vitamin K. Certain bacteria act as decomposers and decompose dead material into simpler forms which are used as nutrients by plants. Bacteria that cause milk to become sour are used to make cheese and yogurt. Vinegar is produced by the action of bacteria on ethyl alcohol.

Certain bacteria cause adverse effects in the body, leading to disease, and are called pathogens.

2. *Viruses*

Viruses are ultramicroscopic bodies which cannot be visualized by an ordinary light microscope. The size of virus particles is determined by X-ray diffraction technique and electron microscopy. There are three types depending on morphological arrangement.

Those with cubic symmetry, e.g., **adenovirus**; those with helical symmetry, e.g., **orthomyxoviruses** and those with complex structure, e.g., **pox viruses**.

Viruses are made up of the core of nucleic acid enclosed in a spirally arranged wrapper of specific proteins called **capsid**. Surrounding both these is an external lipid membrane called **envelop**. Viruses are classified as RNA viruses and DNA viruses, depending on the presence of RNA and DNA. RNA viruses are mumps, measles, enterovirus, influenza virus, etc. Adenovirus and pox virus are examples of DNA viruses.

Viruses are obligatory parasites. They multiply only in living susceptible cells. They are host specific and cell specific. Neither host nor cell is changeable. Hence, they are also classified according to the tissue they attack, e.g., CNS is affected by neurotropic viruses, e.g., rabies; skin and mucus membrane are affected by a dermotropic virus, e.g., in chicken pox.

The virus first gets attached to the cell membrane of the host cell. It then enters the cell and loses the envelop and capsid. Nucleic acid undergoes replication and transcription. Translation also takes place and new RNA and DNA strands are formed. This is termed **assembling**. The procapsid with RNA and DNA are now covered by the protein layer capsid and finally the envelop is also formed leading to the formation of a new virus.

Viruses are susceptible to heat and can be destroyed if exposed to 60°C for half an hour. They can be stored at subfreezing temperature and are inactivated by X-ray irradiation.

Viruses produce various types of reaction in the tissues. Some produce inflammatory reactions while some produce inclusion bodies.

Viruses are antigenetically specific. They have hemagglutinating, complement fixing and neutralizing antigens.

AIDS is caused by a typical type of virus, viz., the Human Immunodeficiency (HIV) Virus Type I.

3. *Protozoa*

Protozoa are unicellular organisms. They have a nucleus and cytoplasm but lack a cell wall. They occur in colonies. They move with the help of flagella or pseudopodia. Some cause disease in animals and humans. Some live as obligatory parasites and cause disease in humans. *Entamoeba histolytica* causes amoebic dysentery and the plasmodium vivax causes malaria.

4. *Fungi and Molds*

These are vegetative cells. Fungal diseases, e.g., moniliasis are caused by them.

5. *Helminths*

Tapeworm, roundworm, threadworm, etc., are examples of worm infestation.

19.1.2 Spread of Infection

Germs spread through air or environment, through contact between people and through contaminated food and water.

Infections are caused by bacteria, viruses and other microorganisms. They are found in water, soil or air; in or on human beings, in body secretions; and droplets generated by coughing, sneezing and speaking.

Infection can spread by different means.

Feces are an important source of spreading infection. Germs causing diarrhea or gastroenteritis are found in feces. Stool may contaminate food, water, hands, surfaces and objects.

Droplet spread is another mode of spreading infection. Germs causing cold, sore throat, diphtheria, etc., are found in the secretions of the mouth and nose. On sneezing, coughing and speaking, minute droplets are expelled into the atmosphere. When inhaled by a healthy person or if it lands on the eye, nose or mouth, it causes infection. Some viruses survive in the environment for a long time and can cause indirect spread.

Infections, especially skin infections, are spread by **direct contact**. AIDS and syphilis can spread through sexual intercourse.

Skin is an excellent barrier to the spread of infection. If there is a break in the skin, infection can spread by direct contact with blood or with mucous membrane. If the blood of an infected person soils clothes or objects, it can spread infection.

Water contaminated with germs, especially of diarrhea or dysentery, can spread infection. Waters of ponds, rivers and lakes are good breeding areas for germs and hence diarrhea and dysentery are more common in the monsoon.

Food can be directly contaminated by handling with infected hands or indirectly through flies, dust, excreta of insects or dirty water.

Dust and air can both spread diseases. Certain germs, e.g., those of tuberculosis, survive in the atmosphere for a long time and blowing winds can carry them to other places.

Milk is another source of spreading infection. Tuberculosis, especially bovine tuberculosis, spreads through cow's milk.

Fomites can spread infection when used commonly. If a handkerchief of a patient, who has cleaned his nose, is used by another person, he can get the infection. Same utensils, if used, can spread infection. Clothes, furniture, thermometers, etc., can spread infection.

Vectors are common culprits in spreading infection. Flies spread typhoid, diarrhea, cholera, etc. They sit on excreta or vomitus of an infected person and then sit on food materials which when eaten, spread the infection.

Mosquitoes spread infection by biting an infected person and sucking his blood. They can then again bite a healthy person and spread diseases like malaria, dengue and yellow fever.

Certain parasites bite and transmit germs. Plague is transmitted by fleas from the rat on which they live. Mites transmit germs of African tick fever by biting.

19.1.3 Prevention of Infection

As mentioned earlier, one must take good care of one's own health and also of family, friends and community.

Knowledge about various diseases and their prevention is necessary for prevention of infection. This can be achieved by distributing pamphlets, pasting posters, giving lectures, and the best way is through media—newspapers and television. Public awareness is the best way of preventing infection and its spread.

Good personal hygiene requires the following:

- Cover your mouth while sneezing and coughing. Nasal discharge should be collected in tissues and disposed off.
- During food preparation, good hygiene practice is necessary.
- Combs, razors, toothbrushes, towels, etc., should not be shared.
- Eating utensils and drinking vessels should not be shared.
- Children should be taught to wash their hands frequently, especially after play and before eating.
- Staff and residents of hospitals should wash their hands with soap frequently.
- Handwashing is an effective way of preventing spread of infection, especially for those who handle food or those who are in contact with infected people. Those who visit hospitals must wear a mask, gloves and gown before visiting patients. One must wash hands after using the toilet, after handling garbage or handling an animal, before eating, after changing a diaper or cleaning a child who has used the toilet.
- Those in contact with patients must be properly screened so that they do not become carriers. They should be vaccinated. Those in contact with patients of tuberculosis must be X-rayed and their sputum examined for presence of acid fast bacilli.
- Vaccination can also prevent infections. Those who are at increased risk of developing infection like children, older people and those with less immunity should be vaccinated. Immunization is of great value in preventing spread of infection, and sometimes mass immunization may become necessary to prevent epidemics.
- Keeping surfaces and items clean helps reduce the spread of infections.
- Workers in factories, children in schools and students in colleges must undergo medical examinations regularly so that any person having a subclinical infection can be detected and treated. This also helps prevent further spread of infection.
- Certain diseases are infectious and spread fast and easily. Hence, they should be notified to the health authorities.

They are measles, chickenpox, smallpox, tuberculosis, poliomyelitis, leprosy, AIDS, infectious hepatitis and cholera.

When a person gets an infectious disease, he has to be isolated. The person nursing him must be vaccinated, must keep away from cooking, must not handle food and must wash his hands before eating.

Sometimes quarantine may be necessary to prevent spread of infection.

- **Disinfection** is a good method of preventing diseases.

  Sunlight and fresh air are **natural methods** of disinfection.

  Physical methods like boiling, steaming and burning are also helpful in preventing diseases.

  Chemical methods are used in solid, liquid or gaseous form. Soap is a good example of a solid disinfectant used to wash hands. Liquids are used to disinfect urinals, floors, spittoons, etc. For disinfecting rooms, gaseous disinfection is the best method. Vapor sterilization at high pressure, as in an autoclave, helps sterilize instruments used in surgical and medical procedures. Freeze cooling suppresses growth of germs but does not kill them.

  Despite significant progress in preventing and treating infectious diseases, they remain a major cause of illness and death, especially in places of poor nutrition, poor sanitation and crowding.

19.2 CERTAIN USEFUL TERMS

Sporadic Diseases occurring at irregular intervals, or appearing singly or scattered here and there or occurring isolated are called sporadic diseases.

Endemic A disease which occurs regularly in a particular area, is prevalent in or peculiar to a particular locality, region, or people is said to be endemic, e.g., malaria is prevalent in many tropical countries. Filariasis is common in Surat. The disease is native to a specific region or environment and does not occur anywhere else.

Epidemic A disease that affects more people than usual in a particular area and spreads rapidly and also disappears rapidly is an epidemic. Some few years back viral conjunctivitis was an epidemic in Mumbai affecting millions. It also disappeared equally fast. Viral hepatitis is another example of an epidemic.

Pandemic A pandemic is an epidemic of an infectious disease that spreads across a large region or even a continent or even worldwide. A disease or condition is not pandemic just because it is widespread, but it must also be infectious.

Contacts Contacts are persons who have been in contact with an infected person and harbor germs but may or may not suffer from that disease.

Carriers Carriers harbur germs and infect others but they do not suffer from the disease. They discharge the germs at regular intervals.

When a patient recovers from an infectious disease, he discharges germs which could infect those in contact with him. He is a convalescent carrier. He could be a temporary carrier as he infects others for a short period, e.g., viral infection. If he discharges germs for a very long time—even months or years—he is a chronic carrier, most commonly seen in a tuberculous patient.

Incubation That interval between the entry of germs into the body and appearance of disease is called incubation period.

Quarantine Those who have been in contact with infected persons are kept in isolation and not allowed to mix with others for the incubation period of that disease. This is called quarantine.

Host and Parasite When an organism is dependent on another and multiplies in it then it is called a parasite, and the organism which allows the parasite to grow in it is called the host.

Fomites Objects or material which get contaminated on coming in contact with an infected person are called fomites, e.g., handkerchief, furniture, bed.

Vectors Vectors are intermediate hosts which spread diseases. They could be mechanical vectors and biological vectors. Mechanical vectors indirectly spread diseases. Flies sit on dirt and excreta and then sit on food and transmit disease. Mosquitoes are examples of biological vectors which cause malaria.

19.3 COMMUNICABLE DISEASES

Communicable disease is the term used for an illness which is transmitted from person to person directly or indirectly. The causative organism or its product spreads either by direct contact of a healthy person with a sick person or indirectly through food or environment or even through a vector.

Mentioned below are the few examples of various communicable diseases and their route of transmission.

- **Direct-contact diseases**: skin diseases and venereal diseases.
- **Water-borne diseases (which can spread through water and food)**: typhoid, cholera and gastroenteritis.

- **Air-borne diseases (which spread through air)**: tuberculosis, other respiratory diseases.
- **Insect-spread diseases**: dengue, malaria.

There is a phase or period before the infectious agent can cause disease in the healthy person. This is termed the **communicable period.**

19.3.1 Water-borne Diseases

Contaminated water (with pathogens or excreta of an infected person) if consumed, leads to certain diseases.

Table 19.2 *Water-borne diseases*

Infecting Agent	*Diseases*
Viral	Hepatitis, poliomyelitis, etc.
Bacterial	Gastroenteritis, typhoid, dysentery, etc.
Worm infestation	Roundworm, hookworm, tapeworm, etc
Protozoal	Amoebiasis, giardiasis, etc.
Toxic substances	Copper, lead, mercury, etc.

Spread of Disease

The diseases are transmitted by a healthy person coming in direct contact with a sick person or a carrier or one who is convalescing.

Transmission could be fecal–oral route. Food, milk, fruits, drinks can get contaminated with the feces, vomit or urine of the infected person and if this is consumed, the disease gets transmitted.

Fomites like clothes, utensils, books, etc., spread infection. Bacteria can survive for many days on fomites.

Flies sit on excreta or contaminated food. Pathogens get attached to its legs and when these flies sit on other (non-contaminated) food materials, they contaminate it. This on consumption can cause disease.

Preventive Measures

Public awareness is the most important and best way of preventing diseases. The disease should be notified to the public by health authorities.

Educating through posters, media like TV and newspapers, leaflets and cinema slides should be carried out.

The patient should be hospitalized if necessary or placed in a separate room (quarantine). His clothes should be washed in a disinfectant solution and utensils should be washed separately and in boiled water. The person taking care of the patient must take care and wash his own hands thoroughly with a disinfectant.

The patient's excreta (stool, urine and sputum) should be collected in a closed vessel containing phenol and disposed of properly or buried.

Water should be boiled before drinking or should be sterilized by chlorination. Vegetables and fruits should be thoroughly washed before use. Food should be thoroughly cooked. Ice cream, raw vegetables and over-ripe food should not be eaten.

Vaccines, which are available, should be taken. Cholera, polio, hepatitis, MMR and typhoid vaccines are available. Those in contact with the patient—family members and nurses—should also be vaccinated.

Gastroenteritis and dysentery should be treated thoroughly as they are vulnerable regarding carrier state.

1. Cholera

Causative agent *Vibrio cholerae*
Pathology Small intestine is affected, exotoxin is secreted leading to outpouring of fluid
Symptoms and signs Severe diarrhea, vomiting, leg cramps, pain in abdomen, oliguria and dehydration
Treatment Rehydration should be done immediately to prevent kidney damage

2. Enteric fever

Causative agent *Salmonella typhi*
Pathology Localize in lymphoid tissue of small intestine and Peyer's patches and can even cause intestinal perforation
Symptoms and signs Fever, vomiting, diarrhea, headache, backache, weakness, tiredness, slow pulse, drowsiness, patient may become delirious
Treatment Complete rest, antibiotics like ciprofloxacin, cefexime and chloramphenicol, lots of liquids and fruit juices

3. Amoebiasis

Causative agent Entamoeba histolytica
Pathology Cysts are ingested in contaminated water and food, trophozoites invade colonic epithelium and produce ulcers in the submucosa, in liver causes abscess
Symptoms and signs Abdominal cramps, diarrhea with mucus and blood, flatulence and painful spasms of anal sphincter
Treatment Rehydration, symptomatic treatment for abdominal pain, metrogyl, ornidazole, etc.

4. Diarrhea

Causative agent	*Giardia intestinalis, Cl. Welchii*
Pathology	Damage to the intestinal mucosa and outflowing of fluid
Symptoms and signs	Watery stools, abdominal cramps, thirst and oliguria
Treatment	Rehydration, oral fluids, lopamide

5. Poliomyelitis

Causative agent	Polio virus
Pathology	Access to CNS via mouth, oropharynx, brain stem and spinal cord affected
Symptoms and signs	Fever, sore throat, bodyache, motor-neuron damage leading to weakness and paralysis
Treatment	No specific treatment, complete rest, antibiotics to prevent respiratory infection, physiotherapy

6. Infective Hepatitis

Causative agent	Hepatitis virus
Pathology	Infiltration by lymphocytes and monocytes of the lobules of liver, degeneration and necrosis and in uncomplicated cases regeneration, otherwise destruction of framework
Symptoms and signs	Fever, headache, chills, weakness, upper abdominal pain, nausea and vomiting, passing dark-colored urine and jaundice
Treatment	Symptomatic treatment, avoiding fatty food, gamma globulin should be given in the early phase

19.3.2 Air-borne Diseases

Air-borne diseases are caused by microbes which are inhaled through air, dust, nasal secretions or droplets of saliva.

These diseases are bacterial and viral. Bacterial diseases are pneumonia, tuberculosis, diphtheria, whooping cough and all other upper-respiratory-tract infections. Viral infections are measles, chicken pox, small pox, influenza, etc.

Spread of Disease

The most common mode of transmission is by coming in contact with the sputum or discharge of the patient or carrier.

Sneezing, coughing or even speaking by the patient can lead to expulsion of droplets and spread of infection.

Dust, which contains microbes from droplets or sputum of infected patients, is a common source of spreading infection.

Using utensils used by the patient can spread infection.

Flies infect food and drink and spread infection.

Tuberculosis is one of the most common diseases in India. It can spread directly through sputum, dust, cough, air and commonly through cow's milk. Contact with a patient having this disease also leads to contracting it. Poverty, overcrowding, malnutrition, lowering of immunity and not taking treatment on time also leads to getting this disease.

Smallpox, chickenpox and measles can also easily spread if a healthy person comes in contact with patients and through environment.

Preventive Measures

The most important factor is informing the health authorities. The patients should be hospitalized or isolated. Immediate treatment should be started.

Sputum, secretions from mouth and fomites used by the patient should be disinfected.

Educating the masses is very important. The patients and their relatives should be informed about the disease and about its preventive measures such as not to spit anywhere but to spit in the spittoons. Nasal discharges should be collected in tissues or handkerchiefs. While sneezing and coughing, the mouth and nose should be covered.

Isolation of babies and children having tuberculosis is necessary and other children should not be allowed to go near them. Breast-feeding by a tuberculous mother may be avoided, and these children should also be vaccinated and may be given prophylactic isoniazide medicine.

Overcrowding should be avoided. Proper ventilation and good cross-ventilation in the house is a must. If there is a person in the house with the disease then he should not be allowed to move freely in the house. His clothes and utensils should be separate and also washed separately. The house must be disinfected by the fumes of *neem* leaves. Articles should be disinfected in the sun.

The dead body of a patient should be covered with a cloth containing formaldehyde solution and the body should be disposed of immediately.

Revaccination of the patient and vaccination of the family members, as deemed necessary should be carried out.

Workers at factories and industries; students and children at schools, colleges and institutions should undergo medical check-ups regularly and doubtful cases should be screened or X-rayed.

1. Tuberculosis

Causative agent	*Mycobacterium tuberculosis*
Symptoms and signs	Cough, loss of appetite, loss of weight, evening rise in temperature,

	affects the lungs chiefly; lymph nodes, bones, meninges, intestines can also be affected
Treatment	Chemotherapy with Streptomycin, Rifampicin, Isoniazid, Ethambutol, Pyrazinamide

2. Common Cold

Causative agent	Filterable virus
Symptoms and signs	Headache, body ache, running nose, sneezing, watering of the eyes and sometimes fever
Treatment	No specific treatment, analgesics

3. Influenza

Causative agent	Filterable influenza virus
Symptoms and signs	Fever, chills, body ache, cough, gastroenteritis and could be complicated by bronchitis, pneumonia and ear infection
Treatment	No specific treatment, analgesics, anti-tussives and antiviral drugs may be given

4. Whooping Cough

Causative agent	Gram negative bacteria *Bordetella pertusis*
Symptoms and signs	Cold, running nose, irritating cough producing a characteristic sound, red watering eyes and vomiting
Treatment	Erythromycin, anti-tussives

5. Diphtheria

Causative agent	Gram positive bacillus *Corynebacterium diphtheria*
Symptoms and signs	Fever, difficulty in swallowing, grayish yellow patches in the throat and on the tonsils, toxemia
Treatment	Diphtheria antitoxin given intramuscularly, Penicillin or Erythromycin

6. Measles

Causative agent	Paramyxovirus group called rubella virus
Symptoms and signs	Fever, running nose, red watery eyes, laryngitis, white spots on the inner side of cheeks, red macular rashes on the face, neck back and whole body which subside in 5 to 7 days
Treatment	No specific treatment, prevention is necessary by injecting live attenuated measles virus, active immunization; passive immunization is by giving gamma globulin

7. Chickenpox

Causative agent	Varicella zoster virus
Symptoms and signs	Fever, rash, itching, pustules filled with pus and when dry leave scabs
Treatment	No treatment, prevention is by passive immunity with V-Z immunoglobulin within 72 hours of exposure

8. Smallpox

Causative agent	Variola major in India and variola minor in America
Symptoms and signs	Fever, chills, headache, bodyache, skin lesions in the form of papule, vesicle, pustule, crusts and scabs
Treatment	No treatment, prevention is by vaccination and practically this disease is nearly eliminated

19.3.3 Arthropod-Borne Infection

Many communicable diseases are spread through insects (arthropods) which act as vectors.

Table 19.3 *Arthropod-borne diseases*

Arthropod	*Diseases transmitted*			
	Bacterial	Viral	Protozoal	Miscellaneous
Mosquito		Dengue, yellow fever	Malaria	Filariasis
Sand fly		*Kala azar*		
Housefly	Cholera, typhoid, diarrhea, dysentery, anthrax	Conjunctivitis, poliomyelitis	Amoebiasis	Worm infestations, trachoma
Ticks	Typhus	Encephalitis		Scabies
Lice				Pediculosis, relapsing fever, typhus
Fleas	Plague			Typhus
Cyclops				Typhus
Mites	Relapsing fever			

Spread of Disease

Disease can be spread by arthropods by direct contact, mechanical transmission and by biological transmission.

Arthropods are directly transferred by close contact from person to person, e.g., in pediculosis.

Diseases like diarrhea, dysentery, enteric fever are transmitted by arthropods through an agent. This is **mechanical transmission**.

Biological transmission is a process by which the causative organism multiplies in the arthropod host. Malaria, plague, filariasis are caused by biological transmission.

Control of Arthropods

(a) Environmental Control Elimination of breeding places is the best method of arthropod control. Health education is very important for preventing diseases. Drainages must be closed, water supply and drains should be at far distances and houses should be kept clean inside and outside. Screening of buildings, hospitals and offices by meshed doors can prevent insects from entering. Mosquito repellants also help keep insects away.

(b) Biological Control Certain aquatic animals like larvivorous fish, gambusia and certain fungus feed on mosquito larvae. Hence, if they are grown in water it will decrease mosquito larvae.

(c) Chemical Control Insecticides are used to spray houses and also general roads, cowsheds and stables. DDT is the commonest insecticide and used in the concentration of 1–2 g per square meter area. Chemicals belong to organochlorine, organophosphorus and carbonate compounds. Besides these, other insecticides are Paris green, indalone, sulphur dioxide, prothrin and hydrogen cyanide. Nowadays, a number of arthropods have starting showing resistance to these insecticides. They also cause environmental pollution. Hence, biogradable and less toxic compounds like methoxychlor are replacing highly persistent insecticides.

(d) Genetic Control Genetic methods like cytoplasmic incompatibility, sterile male technique and chromosomal translocations have been found effective in the control of arthropods.

(e) Recent Newer Methods They are still under research. They are sex attraction, insect growth regulators and chemosterilants.

19.3.4 Rodents

Rodents cause damage to human beings, buildings and food. They cause various bacterial (plague), viral (encephalitis), parasitic (amoebiasis), rickettsial (scrub typhus) and other (ringworm) diseases.

They transmit diseases directly through rat bite. They also transmit through rat fleas and by contaminated food or water.

Control of Rodents

Sanitary Measures Proper storage of foodstuff, proper collection and disposal of garbage and construction of rat-proof houses and warehouses help decrease rat menace. Destruction and blocking of rat burrows should be carried out.

Trapping Trapping and destroying the rats is a temporary measure. The wonder trap developed by Haffkin Institute of Mumbai traps 25 rats at a time.

Rodenticides Barium carbonate and zinc phosphide are administered singly or in multiple doses. Single doses prove lethal while multiple doses are given over a period of 3 days.

Fumigation Calcium cyanide, carbon disulphide, sulphur dioxide and methyl sulphide are used to kill rats and rat fleas.

Chemosterilants They cause temporary or permanent sterility in either or both sexes of the rodents.

19.4 MALARIA

Malaria is a protozoal disease caused by the malarial parasite plasmodium. There are four species—vivax, falciparum, ovale and malariae. Vivax and falciparum account for most of the cases. Malaria is transmitted by the bite of the female anopheles mosquito.

Spread of Malaria

There is no natural immunity against malaria and all races are susceptible except negroes who are immune to malaria. Incidence of malaria is more where there is more breeding of mosquitoes. It is seen more in the rainy season where water gets collected and more in marshy soil, rice-cultivation areas, ponds and canals.

19.4.1 Life Cycle of the Malarial Parasite

1. Asexual Cycle

(a) Pre-erythrocytic Schizogony When an infected female mosquito bites a person, it injects sporozoites with its salivary fluid. The salivary fluid prevents clotting of blood at the site of bite. Now blood is sucked. Parasites go to the liver and then re-enter blood and invade the circulating RBC.

(b) Erythrocytic Schizogony The parasite passes through the stages of trophozoite, schizont and merozoite in the RBC. When the RBC ruptures, merozoites are liberated and at this

stage, clinical symptoms appear. The interval between mosquito bite and appearance of symptoms is called incubation period, which is about 14 days.

(c) Exoerythrocytic Phase The liberated merozoites infect fresh RBCs and liver cells, where they multiply and liberate metacryptozoites.

(d) Gametogony Some merozoites undergo meiotic division and form male and female gametes. These male and female gametes do not unite in the host. When the female anopheles mosquito bites such a person, it ingests these gametocytes along with asexual forms of the parasite, which reaches the stomach of the mosquito and forms male and female gametes.

2. *Sexual Cycle*

The male and female gametes unite, fertilization takes place and a zygote is formed. A cyst forms around the zygote which is called **oocyst**. The phase of gametogony starts in the body of human beings and is completed in the body of the mosquito.

(a) Sporogony From the oocyst, after undergoing various changes, sporozoites are formed. They are discharged from the stomach into the esophagus of the vector and reach the salivary glands. On biting a healthy person, sporozoites are injected and the cycle starts again.

(b) Clinical Symptoms Fever with rigors followed by sweating, nausea, vomiting and headache are the common symptoms. Then there is a feeling of warmth followed by marked sweating.

There is anemia, and the spleen and liver are enlarged.

19.4.2 Prevention of Malaria

The most important measure is to prevent the collection of rain water. Water should not be allowed to collect near the house as mosquitoes breed in stagnant water. Wells, tanks and canals should be kept clean or should be kept covered.

Mosquitoes should be destroyed. Various methods are available for this. DDT, if used even in small quantities, destroys them but is rarely used nowadays. Kerosene or diesel oil, if sprayed on the water surface, kills mosquitoes. Gammexane prevents mosquito breeding in wet crops. Larvicidal fish, if put in water, help to prevent mosquito breeding.

Another very important aspect of preventing malaria is to prevent mosquitoes from biting. Wire netting in doors and windows are helpful. Hands and legs, especially in children, should be well covered. Mosquito repellants, if applied on the body, prevent mosquitoes from biting.

Parasiticidal drugs are used for treating malaria as well as prophylaxis. They kill the parasites when they are circulating in the blood. The drugs are Camoquine, Quinine, Chloroquine, Sulphamethoprim or Daraprim.

Carriers should be detected and given parasiticidal drugs. During epidemics, antimalarial drugs should be distributed by the municipality to the public.

19.4.3 Other Diseases

1. *Filariasis*

Causative agent	*Wuchereria bancrofti, B. malayi*
Symptoms and signs	Fever, swelling of the hands, legs, scrotum, lymphangitis, lymphadenitis
Treatment	Diethylcarbamazine, corticosteroids, antihistaminics, and if necessary plastic surgery

2. *Dengue*

Causative agent	Mosquito *Aedes aegypti*
Symptoms and signs	High fever, frontal headache, stomach ache, vomiting, cold clammy skin, bleeding from nose and mouth, excessive thirst
Treatment	No specific treatment, symptomatic treatment for fever and pain

3. *Rabies*

Causative agent	Viral—rabdo virus group and caused by the bite of rabies infected dogs
Symptoms and signs	Hydrophobia, excessive salivation, fever, muscle spasm, terminal hyperpyrexia
Treatment	General care, sedatives, control of respiration and cardiac failure, rarely anyone survives

4. *Plague*

Causative agent	*Pasteurella pestis*
Symptoms and signs	High fever, headache, aching swollen lymph nodes—bubonic plague Overwhelming infection, pneumonia, meningitis—septicemia plague Cough, dyspnea, hemoptysis, cyanosis and even fatal—pneumonic plague
Treatment	Tetracycline, Streptomycin, Clotrimoxazole, Chloremphenical, Sulphadiazine Vaccination and chemoprophylaxis with tetracycline to contacts

5. Tetanus

Causative agent	*Clostridium tetani*
Symptoms and signs	Fever, headache, restlessness, stiff neck, lockjaw, rigidity, convulsions
Treatment	Tetanus toxin, wound treatment, Penicillin, to avoid spasms patient kept in a quiet, dark room, Diazepam I/V

6. Leprosy

Causative agent	*Mycobacterium leprae*
Symptoms and signs	Small patches on the skin, thickened and wrinkled, facial skin, swollen ears, nasal and throat discharges contain the bacilli and are infectious, deformities of hands and legs, peripheral neuritis
Treatment	Rifampicin, Clofazimine, Dapsone, given for a long period

19.5 WORM INFESTATION

Worms are triploblastic animals. They consist of three parts—epiblast, hypoblast and mesoblast. They are classified as nematodes, cestodes and trematodes.

Nematodes are slender worms with no segments. They have an alimentary canal with the mouth at one end and anus at the other end, e.g., roundworm, hook worm and threadworm.

Cestodes are flat, segmented worms, e.g., tapeworm.

Trematodes are flat and variously shaped, e.g., liver fluke and schistosoma.

1. Roundworm

Characteristics	Cylindrical, pinkish grey, female lays eggs which are swallowed with food, water, etc., shell dissolves in small intestine, embryo reaches heart and lungs via circulation, re-enters intestine via trachea and esophagus and develops into adult worm
Preventive measures	Personal hygiene, excreta of infected person should be disposed off properly, vegetables and fruits should be washed properly
Treatment	Piperazine, Levamisole, Mebendezole, Pyrantel palmoate

2. Hookworm

Characteristics	Cylindrical, female lays eggs in intestine and excreted with feces, larvae develop in soil and enter through subcutaneous tissue and reach lymphatics or circulation, or enter via mouth and go to the intestine and get attachéd to mucous membrane and suck blood
Preventive measures	Foot protection by wearing footwear, personal hygiene, water contamination should be prevented, carriers and infected persons should be treated properly
Treatment	Bephenium, Pyrantel palmoate, Mebendezole, Thiabendezole

3. Threadworm

Characteristics	Very small, eggs enter GI tract by taking contaminated food, shell dissolves in small intestine, larvae enter into cecum, female lays eggs near anus and on scratching there is reinfection through fingers
Preventive measures	Auto-infestation prevented by keeping clean, short nails, hands washed properly after toilet and before eating, infected children should be properly treated, ammonium mercury ointment should be applied to prevent itching
Treatment	Thiabendezole, Mebendezole

4. Guineaworm

Characteristics	Threadlike, burrows under the skin mostly legs, blister forms and breaks and female comes out, larvae pass into water and Cyclops eat it and when water infected with these Cyclops is taken, infection occurs
Preventive measures	Water should be disinfected with potassium permanganate, drinking water should be boiled or filtered water should be drunk, one must not enter wells and tanks, persons suffering from this infection should not handle drinking water
Treatment	Physical removal of worm, antihistaminics, antibiotics for secondary infection

5. Tapeworm

Charecteristics	Flat with head, neck and segments, excreted with feces and ova are eaten by animals (pig and cattle), shell dissolves in the intestine and embryo is formed which fixes to the mucosa through hooks and develops into adult worm
Preventive measures	Infected persons should be treated, proper cooking of meat and fish, must not eat raw meat, proper disposal of excreta
Treatment	Niclosamine, Diclorophen

6. Liver fluke

Charecteristics	Heart-shaped and flat, sheep is the host
Preventive measures	Infected persons should be treated, avoid drinking and bathing in infected water, sterilize water with copper sulphate
Treatment	Albendazole, triclabendazole

7. Schistosoma

Charecteristics	Very small, 1 cm long, produces infection in bladder, intestine, ureters and kidney
Preventive measures	Infected persons should be treated, avoid drinking and bathing in infected water, sterilize water with copper sulphate
Treatment	Praziquantel

19.6 SEXUALLY TRANSMITTED DISEASES

Sexually transmitted diseases are communicable diseases transmitted by sexual intercourse with an infected person.

1. Syphilis

Causative agent	*Treponema pallidum*
Pathology	Hard core called chancre on genital—primary stage; headache, fever, lymph node enlargement, loss of hair—secondary stage; multiple organ involvement, gumma—tertiary stage
Symptoms and signs	Skin and mucous membrane invaded, then organisms enter lymphatics and blood and systemic infection and metastatic foci
Treatment	Procaine penicillin

2. Gonorrhea

Causative agent	*Neisseria gonococci*
Pathology	Mucous membrane of pharynx, urethra, cervix, anus, survive in Fallopian tubes in females and seminal vesicles, epididymis, prostate in males
Symptoms and signs	Pain and pus discharge while passing urine, muscles, joints, eyes and meninges affected with inflammation
Treatment	Procaine penicillin

3. AIDS

Causative agent	Human immunodeficiency virus
Pathology	Attacks organs of immune system having protein receptor CD4, macrophages and dendritic cells also infected, when enough cells are killed cellular immunity is lost
Symptoms and signs	Susceptible to infection, fever, swelling in the groins, cough, dermatitis, Kaposi's sarcoma
Treatment	Azidothymidine, treatment of secondary infection

19.7 FAMILY PLANNING

A family comprises a married couple and their children. Family planning allows couples to plan the required number of children they desire. They can anticipate the spacing and timing of the birth of children and for that they can use various birth-control measures.

Family planning is sometimes wrongly used as a synonym for the use of birth control but it also includes sterilization and pregnancy termination.

Family planning is achieved through use of contraceptive methods and treatment of fertility.

19.7.1 Benefits of Family Planning

A woman's ability to space pregnancies and limit the number of children helps regain her health and strength and has an impact on her well-being and on the outcome of each pregnancy.

Raising a child requires significant amount of resources—social, financial and time. Planning allows these resources

to become available. Having one or two children makes it possible to feed, clothe, educate and bring up the children in a better way.

A woman should wait at least till she is 18 years old so that she is physically fit to maintain the fetus in her womb, leading to proper maternal and child health. After one child, it is healthier, both for the child and mother, to wait at least for 2 years before planning for the second child. After a miscarriage, a woman must not have another pregnancy before 6 months.

Family planning preserves the health of the child and mother. It gives time to parents and children to spend more time with each other. It not only helps the family but also the society, state, and the country socially, economically, culturally and medically and helps the nation to prosper.

19.7.2 Population Problems

With the progress in humanity, both economically and medically, and with better diagnostic facilities, health education and prevention of diseases, there is decrease in the death rate. It has been found statistically, that there is a steep rise in world population. Many of the troubles currently facing us today have been directly caused by this crisis of overpopulation.

The population problem was first brought to attention by Thomas Malthus. According to him, the economy of a nation grows by arithmetical proportions, while the nation's population grows by geometric proportion. Overpopulation is the biggest problem because it makes every other problem worse and difficult to solve.

Overpopulation does not depend on the density of the population but on the ratio of population to available resources. It can result due to increase in childbirth, decrease in mortality rate due to medical advances, due to immigration (certain countries) and due to health education.

There are more people alive each day than those who died in Japan from bomb attacks. There is a surplus of births over deaths. Hence, birth control is absolutely essential to limit the population, or else population will be limited by natural means like starvation, earthquakes, warfare and pandemic diseases. 20,000 people died in an earthquake in India and the losses were made up before the West heard the news.

Hence, it is essential to control the growth of population and the best way is to limit two children per couple.

Birth control is techniques and methods used to prevent conception or to interrupt pregnancy at various stages.

19.7.3 Methods of Birth Control

Various methods are available and the person chooses the device as suited to him/her.

Nowadays, modern medical advances in family planning are used. Pregnancies are achieved by using donated sperms by artificial insemination and less commonly by in-vitro fertilization. In surrogacy treatment, a woman agrees to become pregnant and deliver a child for another person or couple.

Detailed discussion on contraceptive methods has been done in the chapter on reproductive system.

REVIEW QUESTIONS

1. Define disease. Describe the various types of diseases in brief.
2. Define bacteria. Describe its properties.
3. What are viruses? Write about them in brief.
4. How does infection spread? Describe the methods of preventing infection.
5. Define communicable disease. How are they spread? Write a note on the prevention of these diseases.
6. Name some water-borne diseases. Write about their pathology, signs and symptoms and treatment.
7. How are air-borne diseases caused? How do these diseases spread and what are the preventive measures? Name these diseases and write briefly about each.
8. Mention some arthropod-borne diseases. How do such diseases spread? Write a note on the control of arthropods.
9. Describe the life cycle of the malarial parasite. Write a note on the prevention of malaria.
10. Classify worms. Describe their characteristics, preventive measures and treatment.
11. Describe the sexually transmitted diseases.
12. What is family planning? What are its benefits?
13. What are population problems and how can they be solved?
14. Write short notes on:
    a. Protozoa
    b. Fungi, molds and helminths
    c. Sporadic, endemic, epidemic, pandemic
    d. Contacts and carriers
    e. Incubation
    f. Quarantine
    g. Host and parasite
    h. Vectors
    j. Rodents
    k. Filariasis
    l. Dengue
    m. Rabies
    n. Plague
    o. Tetanus
    p. Leprosy

The McGraw-Hill Companies

Index