International Standard
Colored Edition

Eighth Edition

Volume 1

LPR Fundamentals of Medical Physiology

As per the Competency-Based Medical Education Curriculum (NMC) for the Indian Medical Graduates

What's **NEW** in this Edition?

Thoroughly Revised and Updated Edition as per CBME Curriculum (NMC)

- Most Updated with Recent Advances
- Extensive Coverage of Applied Aspects
- Unique Amalgamation of Theoretical and Clinical Aspects
- Numerical Formulas for Quick Review
- Physiological Problems and Solutions
- Includes Important & Useful Facts
- **1500+** Illustrations and Images
- **1000+** Rapid Review Questions and Answers
- **1000+** Multiple Choice Questions
- **500+** Solved and Unsolved Clinical Case-Based Questions
- **1000+** Rapid Review Points
- Complemented with Numerous Tables and Flowcharts

L Prakasam Reddy

Volume
1

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Eighth Edition

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PREFACE TO THE EIGHTH EDITION

It is a pleasure to bring out the eighth edition of ***LPR Fundamentals of Medical Physiology*** in a completely revised and student-friendly format. This edition has been thoroughly updated based on the latest Competency-Based Medical Education (CBME) curriculum. The entire subject of Physiology is divided into competencies and sub-competencies. Scenario-based and task-based questions are given at the end of each section to enable the students to do the self-assessment test and appear confidently for the exams.

What is Competency?

Competency is defined as "the ability to do something successfully and efficiently." CBME is an approach to ensure that the graduates develop the competencies required to fulfill the patients' needs in the society. Teaching of Physiology to the medical graduates is as per the CBME-2019.

I. Goal

The broad goal of the teaching of undergraduate students in physiology is to provide the student with comprehensive knowledge of the normal functions of the organ systems of the body to facilitate an understand the physiological basis of health and disease.

II. Objectives

A. **Knowledge:** At the end of the course the student will be able to:
   1. Explain the normal functioning of all organ systems and their interactions for well-coordinated total body functioning.
   2. Assess the relative contribution of each organ system to the maintenance of the milieu interior.
   3. Elucidate the physiological aspects of normal growth and development.
   4. Describe the physiological response and adaptations to environmental stress.
   5. List the physiological principles underlying pathogenesis and treatment of the disease.

B. **Skills:** At the end of the course the student will be able to:
   1. Conduct experiments designed for study of physiological phenomenon.
   2. Interpret experimental/investigative data.
   3. Distinguish between normal and abnormal data derived as a result of the tests which he/she has performed and observed in the laboratory.

C. **Attitude and communication skills:** At the end of the course the student will be able to:
   1. Show due respect to the persons who volunteer to be examined for the purpose of learning clinical examination.
   2. Communicate effectively with peers and teachers.
   3. Demonstrate the ability of team work.

D. **Integration:** At the end of the first year integrated teaching, the student should acquire an integrated knowledge of organ structure and function and the regulatory mechanisms and tests to assess the functional status of organ systems.

The student should know the basic features of clinical conditions explained at the end of each chapter. This helps the student in getting ready with the clinical knowledge before he/she enters the portals of hospital.

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EARLY CLINICAL EXPOSURE (ECE)

Concept

Early clinical exposure (ECE) to the first professional medical undergraduates is a method adapted by medical educationists to expose the undergraduate students directly to the patients during their first year course.

It is highly challenging to introduce clinical subjects to first-year undergraduates who are supposed to learn basics in Physiology, Anatomy and Biochemistry. It is believed that this Early Clinical Exposure will make them appreciate the importance of first-year subjects as a part of clinical medicine in their medical career.

Methods in Early Clinical Exposure

ECE can be performed by:

1. **OPD visits:** Students observe how doctor–patient interaction takes place.
2. **Visit to the wards:** Students observe how doctors, paramedical staff and nursing sisters deal with the inpatients.
3. **Case presentation:** The students will be given a case presentation about a system-based module.
4. **Case discussion:** The in charge doctor would explain and discuss the relevant case with the students. For this purpose the students are taken to the wards.
5. **Problem-based learning:** A clinical case scenario on a specific topic is created and a discussion may be initiated with the student active participation.
6. **Demonstrating the clinical-based investigations:** Investigations recorded from the patients should be explained about their recording analysis and significance of their variations.

Advantages

1. It creates interest in the undergraduate students and motivates them to think beyond the first year subjects as they read the disease process.
2. It helps the students to remember the features of the disease, the investigations and the drugs used for the management of a disease.

Probable ECE Modules as per CBME-2019

1. Acute Myocardial Infarction (STEMI, Non STEMI)
2. Parkinsons Disease (PD)
3. Spinal Injury
4. Type 2-Diabetes Mellitus
5. Acid-Base Disorders
6. Obesity
7. Ascites
8. Chronic Obstructive Pulmonary Disease (COPD)
9. Thyrotoxicosis
10. Acid-peptic Disease
11. Hypertension
12. Jaundice
13. Anemia
14. Cushing Syndrome

1 Introduction to Physiology

CHAPTER OUTLINE

- Introduction
- Need for Learning Physiology
- Utility of Physiology
- Scientists' Contribution to Physiology

INTRODUCTION

Physiology means study of the mechanisms and their regulation of body functions in healthy living organisms.

Human physiology: It is the study of various bodily functions in humans brought about by the integrated and coordinated activity of various organ systems in human. Although human physiology is similar to the physiology of other mammals yet it differs from that as the human physiological processes are profoundly influenced by the mindset of the humans.

Medical physiology: It is the application of knowledge of human physiology in bringing back the dysfunctions and diseases to normal levels in human beings.

Clinical physiology: It is the study of functional changes or compensatory mechanisms that occur in human body systems when some parts of the body becomes dysfunctional due to some disease. For example the study of changes in the function of lungs, liver and kidneys whenever the heart fails to pump normally.

NEED FOR LEARNING PHYSIOLOGY

Physiology provides basic knowledge about how a given body function is regulated by the activity of various body systems. Therefore, all homeostatic mechanisms help in maintaining internal harmony among the body systems. Disruption of homeostatic mechanisms leads to a disease a deeper knowledge helps the physician to manage and reverse the disease process easily. *Hence, physiology is called the mother of medicine*. Therefore, it is not surprising to profess "A good physician is primarily a great Physiologist".

UTILITY OF PHYSIOLOGY

The subject of physiology is utilized in most of the medical subjects indicating that it plays an important role in several medical specialties.

Pharmacology: It is an extension of physiology and is also called experimental physiology. This provides information about how drugs, or chemicals alter body function.

Pathology: Proper understanding of pathology requires physiology.

Surgery: A thorough knowledge in physiology would help a surgeon to provide best surgical therapy for the needy persons.

Applied physiology: Knowledge in physiology has wider applications in various branches of science that influence human health. Thus, we have environmental physiology, sports physiology, Nutrition, aviation physiology, space physiology, psychophysiology, deep sea physiology, molecular physiology, etc.

Investigative physiology: Various clinical investigations are utilized to assess the physiological state of different body systems (e.g., ECG, EEG, nerve conduction tests, etc.)

Prevention of disease: By regularly practicing certain Physiological activities like, regular exercise, yoga, regular sleep, controlled food intake, etc. would help in maintaining body functions all within normal range.

Therefore, the science of physiology would help everyone from children to the aged in maintaining their body function within the normal range.

SCIENTISTS' CONTRIBUTION TO PHYSIOLOGY

Sir Augustus D Waller

In 1862, he explained about Wallerian Degeneration in distal part of nerve cut following Nerve Injury.

Sir Otto Frank and Sir Starling Ernest

In 1910, Frank and Starling explained the relation between end diastolic volume (initial length of the cardiac muscle) and force of contraction of the ventricles as Frank-Starling Law of the heart.

Sir Babinski Joseph

Explained about Abnormal Plantar Reflex called Babinski Sign associated with upper motor lesion.

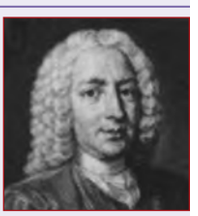
Sir Bayliss Folkow

In 1902, Bayliss Folkow explained that cerebral blood flow is also regulated by the myogenic tone of the cerebral blood vessels called Bayliss Folkow hypothesis.

Sir Bainbridge Kenneth

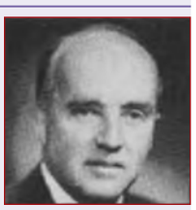
Explained a relationship between increased venous return and heart rate as Bainbridge Reflex in 1918.

Sir Bernoulli Daniel



He proposed that the sum of kinetic energy of flow and the pressure energy is constant when blood is flowing in a blood vessel. Any increase in kinetic energy causes a fall in lateral pressure energy. This is called Bernoulli Principle and is applicable to all the blood vessels with narrowed part at one point.

Sir Banting Frederick and Sir Charles Best



In 1921, Banting and Best discovered Insulin Secretion from pancreas.

Sir Bohr Neil

Sir Bohr explained the role of PCO_2 and H^+ ions on the release of O_2 from HbO_2 in the tissue as Bohr Effect.

Sir Langerhans

A medical student studying anatomy discovered islets in pancreas that secrete insulin and glucagon called Islets of Langerhans.

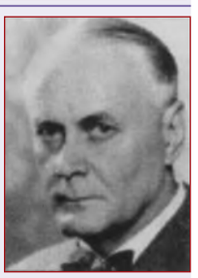
Sir Breuer E and Sir Herring E

Herring E and Breuer E in 1868 explained the role of vagal afferents from the receptors in the lung as Herring–Breuer inflation and Herring Breuer Deflation Reflexes.

Madam Goldman, Sir Hodgkin and Sir Katz B


Madam Goldman, Sir Hodgkin and Sir Katz explained role of distribution of Na^+ and Cl^- ions across the membrane on the magnitude of the membrane potential. The equation is referred as Goldman-Hodgkin-Katz Equation.

Sir Granit J



Sir Granit proposed a theory for color perception called Granits Theory. According to this theory ganglion cells are of two types:

1. Dominators, which respond to the entire visual spectra.
2. Modulators: These are divided into three groups each one responding to one primary color.

Sir Hagen L and Sir Poiseuille J L

Sir Poiseuille and Sir Hagen explained the relation between blood flow, pressure and resistance and the effect of change in radius of blood vessel on blood flow. This is called Poiseuille–Hagen Formula.

Blood flow $Q = \frac{\Delta P}{R}$

Resistance $R = \frac{8L\eta}{\pi r^2}$

Sir Haldane

Sir Haldane explained the effect of PO_2 on the release of CO_2 from the blood into the lungs. This is called Haldane Effect.

Sir Humberger

Sir Humberger explained in 1918 about the changes in RBC and plasma during transport of CO_2 from tissue to lungs. This is called Humberger Phenomenon, also known as $Cl^-HCO_3^-$ shift between RBC and plasma. Cl^- enters RBC while HCO_3^- enters plasma.

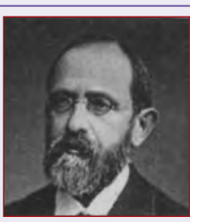
Sir Hans Berger

Sir Hans Berger recorded Electroencephalogram (EEG) by placing electrodes on the scalp. He recorded 'α' rhythm—first from a person with closed eyes and hence 'α' rhythm is called Berger Rhythm.

Sir Harvey Cushing

Sir Harvey explained the features under the heading—Cushing Syndrome and Cushing Disease which are due to increase in secretion of glucocorticoid hormones.

Sir Heidenhain



Sir Heidenhain prepared a vagally denervated pouch of stomach to study the influence of non-neural factors on gastric secretion.

Sir Henry

Sir Henry proposed Henry Law. It states "at a constant temperature amount of gas dissolved in a solution is directly proportional to the partial pressure of that gas."

Sir Heymans C and Sir Neil E


Sir Heymans and Sir Neil discovered the chemoreceptors (carotid body and aortic body) in 1930 and explained their role in the chemical regulation of respiration.

Sir Hensen J

Sir Hensen discovered the H-zone present in the middle of the 'A' band. This region represents non-overlapping region of myosin filaments with actin filaments.

Sir Holmgren

Sir Holmgren utilized Holmgren's Skeins of Colored Wool Test for the detection of color blindness.

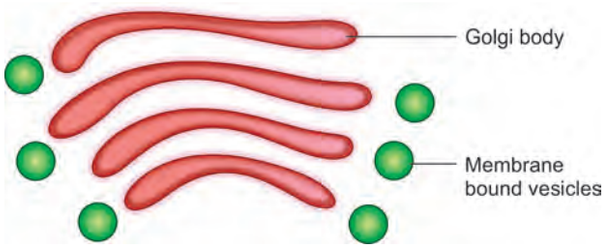


Fig. 2.5: Golgi complex

Functions

- The Golgi complex is responsible for the processing, sorting and delivery of proteins, lipids and carbohydrates to various parts of the cell.
- It also packs the various secretory substances in membrane-bound granules prior to exocytosis. *For example,* neurotransmitter-secreting neuron, exocrine and endocrine cells.
- This is also responsible for the conjugation of lipids, proteins and carbohydrates into the lipoproteins, glycoproteins and glycolipids.
- The Golgi complex also has a role in the production of the membranes of the organelles and their enzymes.
- It also gives rise to lysosomes, peroxisomes and other membrane-bound vesicles.

Processing of endoplasmic reticular secretions by Golgi apparatus into membrane bound vesicles and their fate (Fig. 2.6):

- The various substances formed by the endoplasmic reticulum are packed as membrane bound vesicles, which fuse with Golgi apparatus. Golgi apparatus modify.
- These substances by adding carbohydrate or lipid moieties and packs them as compact membrane bound vesicles that include lysosomes, peroxisomes and secretory vesicles. The lysosomes and peroxisomes remain inside the cells and perform special functions.
- The secretory vesicle contains enzymes, proteins, hormones, neurotransmitters, etc. and empty their contents into the interstitial space by a process called exocytosis.

Lysosomes

These organelles measuring about *250–750 μm in diameter originate from the Golgi complex* and have a thicker membrane than the rest of the organelles, because they contain about 40 hydrolases. *These enzymes are called lysozymes and are capable of breaking nucleic acids, lipids, proteins and carbohydrates.* They are synthesized by rough ER, and processed into lysosomal vesicles by the Golgi complex. *These are found in most of the animal cells except erythrocytes and they act as the digestive system of the cell* (Fig. 2.7).

There are three types of lysosomes:

1. **Primary lysosome:** This is formed directly from the Golgi apparatus. It contains several inactive enzymes.
2. **Secondary lysosome:** The primary lysosome fuses with phagosome or endosome and forms secondary lysosome. The enzymes of secondary lysosome become active.
3. **Tertiary lysosomes:** These contain residual bodies after foods are digested. The enzymes become inactive.

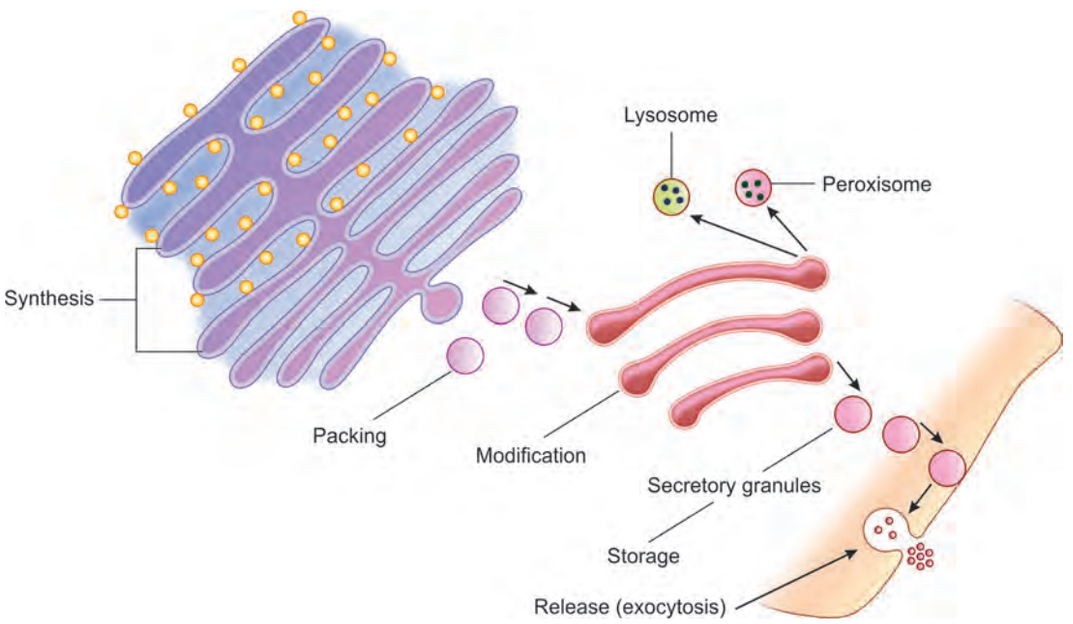


Fig. 2.6: Processing of endoplasmic reticular secretions by Golgi apparatus into membrane bound vesicles

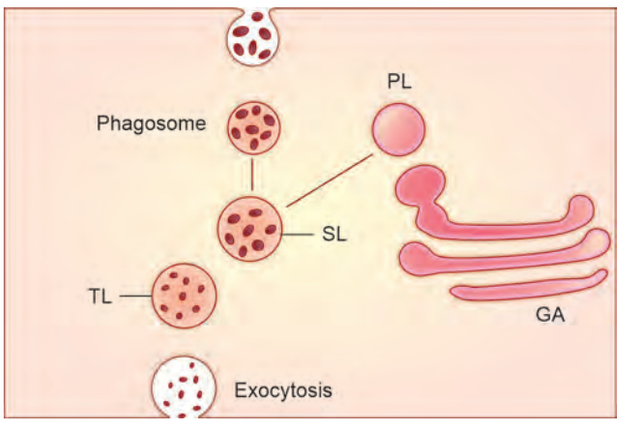


Fig. 2.7: Lysosome

Abbreviations: GA, Golgi apparatus; PL, primary lysosome; SL, secondary lysosome; TL, tertiary lysosome

Functions

- It helps in intracellular digestion of phagocytic or pinocytic substances. Complex substances are broken into simpler substances.
- Destruction of pathogens ingested by neutrophils and macrophages (Heterophagy) (Fig. 2.8).
- Digestion of senile organelles (Autophagy).
- Some special lysosomes called secretory lysosome release some chemicals extracellularly and participate in cytolysis, e.g., lysosomes of cytotoxic 'T' lymphocytes and NK cells secrete perforin and granzymes. Perforin destroys viral infected cells and tumor cells. Granzymes participate in apoptosis.
- **Role in fertilization of ovum:** Acrosome present on the head of sperm is considered as a specialized lysosome. This plays an important role in the penetration of sperm into the ovum.

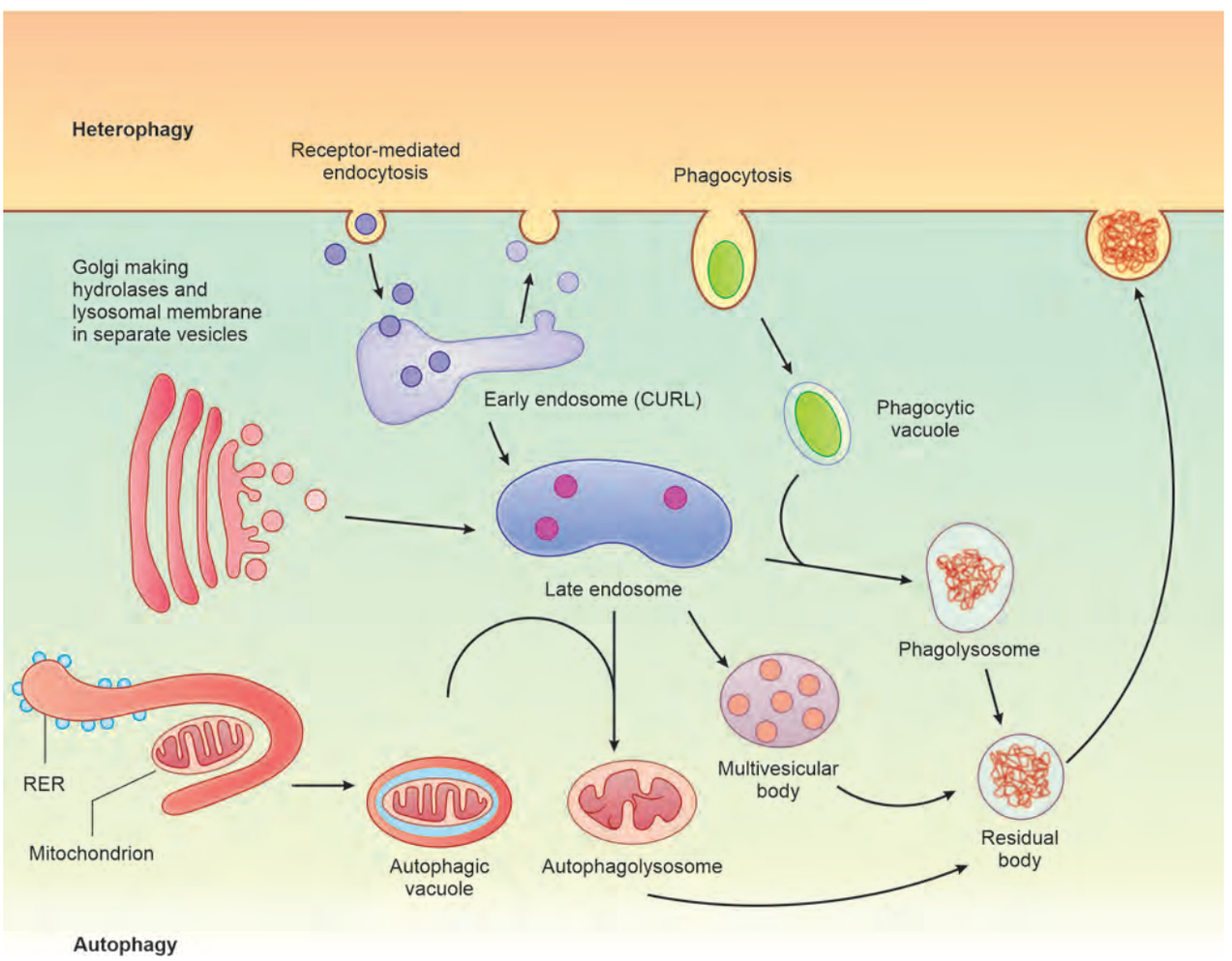


Fig. 2.8: Heterophagy refers to the intracellular digestion of material taken into the cell from outside (top of illustration, whereas autophagy is the digestion of parts of the cell itself (bottom). The different pathways and the types of lysosomes involved in each pathway are shown. RER, rough endoplasmic reticulum.

Applied Physiology

- Release of lysosomal enzymes into cytoplasm can cause self-destruction. This is called **autolysis**. Hence, lysosomes are often called the **suicide bags of the cell**.
- Arthritis, muscle disease, allergic disorders have been attributed to the release of lysosomal enzymes.
- Plasma **acid phosphatase levels are used as a marker for lysosomal activity**.

Clinical Correlation

Lysosomal Storage Disease

Congenital deficiency of lysosomal enzymes leads to increase in the number of non-functional lysosomes in the cell. Hence, the name lysosomal storage disease (Table 2.1). The substances ingested cannot be degraded leading to the impairment of cell function and death.

TABLE 2.1: Common lysosomal storage diseases

Disease	Enzyme deficiency	Features
Tay-sachs disease	β-hexosaminidase-A	Mental retardation Hyperacusis in infants Blindness
Gaucher disease	Acid-β glucosidase	Hepatosplenomegaly Skeletal dysplasia
Fabry disease	α-galactosidase-A	Cutaneous keratoconus Hypolipidosis
Niemann-Pick disease	Sphingomyelinase	Mental retardation Seizures Lung failure

Peroxisomes

These are small ovoid structures present in liver and kidney cells. They develop from smooth endoplasmic reticulum. They resemble the lysosome and contain two types of enzymes—*catalases* and *oxidases.*

Functions

- Catalases convert H_2O_2 into H_2O and O_2 (detoxification).
- Oxidases are involved in breakdown of lipids and alcohol.
- Degradation of nucleic acids and cholesterol.

Clinical Correlation

Peroxisomal Diseases

- **Zellweger syndrome** is a genetic disease in which normal peroxisomes are absent. Infants with this syndrome have profound neurological disorders and liver and kidney problems, and usually die within a few months. Electron micrographs of biopsies from these patients reveal empty peroxisomes, lacking enzymes. Although peroxisomal enzymes may be synthesized, they become dislocated in the cytosol.
- **Refsum disease**—autosomal recessive disorder of α-oxidation → phytanic acid not metabolized to pristanic acid. Scaly skin, ataxia, cataracts/night blindness, shortening of 4th toe, epiphyseal dysplasia.
- **Adrenoleukodystrophy—**X-linked recessive disorder of β-oxidation due to mutation in ABCD1 gene → VLCFA buildup in adrenal glands, white (leuko) matter of brain, testes. Progressive disease that can lead to adrenal gland crisis, coma, and death.

Mitochondrion

The size, shape and the number of mitochondria vary from cell to cell; length varies from 5 μm to 12 μm and width 0.5 μm to 1 μm (Fig. 2.9). Each cell may contain about 2000 mitochondria and the number of mitochondria in a cell is proportional to the metabolic activity of the cell. They have the capacity to multiply due to the presence of DNA and RNA. They are double-membrane organelles. The outer membrane envelops the organelle. The inner membrane is thrown into folds called cristae. This is to increase the surface area. The space between the cristae is called matrix. The inner membrane contains the components of oxidative phosphorylation and electron transport system. The matrix contains the enzymes that participate in citric acid cycle and β oxidation. *Mitochondria have short lifespan like other cell organelles.*

Functions

- Mitochondria are concerned with aerobic metabolism. They metabolize the foods in the presence of oxygen and generate energy, heat, CO_2 and water. The energy is converted and stored as adenosine triphosphate (ATP).
- Mitochondria also contain small amounts of DNA and ribosomes, which help in the production of their own enzymes during stressful states. The DNA is derived from the mother. Hence, mitochondrial DNA controls some characters.
- It produces some enzymes that participate in apoptosis.
- It stores Ca^{++} to some extent.
- It plays a role in detoxification of ammonia especially in the liver.

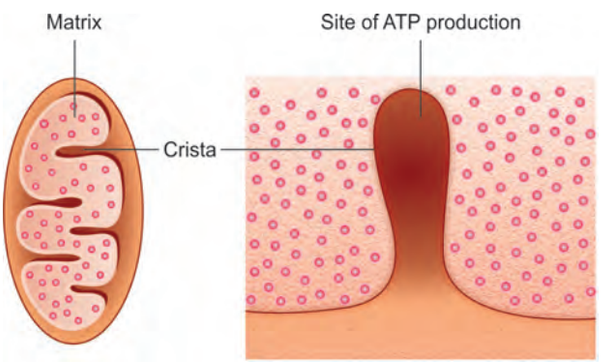


Fig. 2.9: Mitochondrion

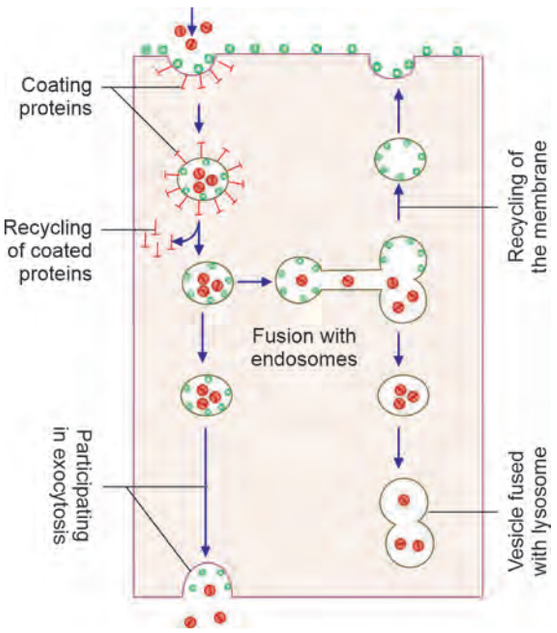


Fig. 4.9: Receptor-mediated endocytosis

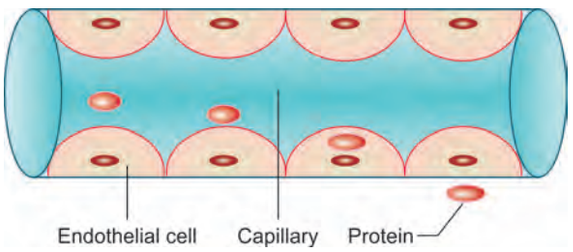


Fig. 4.10: Transcytosis

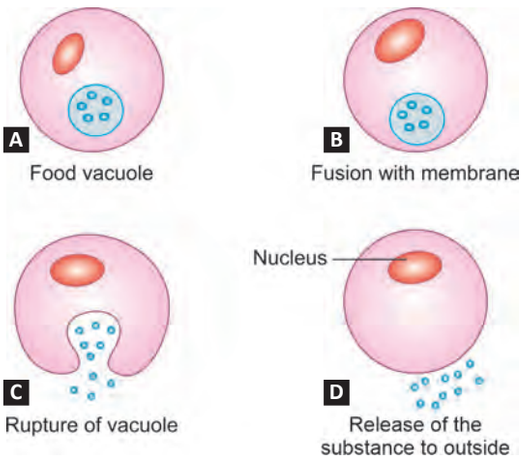
Transcytosis

Small amounts of protein are transported out of capillaries by this process (Fig. 4.10). This involves both endocytosis and exocytosis.

Exocytosis

Exocytosis is the process of discharge of particles from a cell. It is a reverse pinocytosis and is seen in all the cells that secrete protein compounds. The membrane of the secretory granule fuses with the cell membrane and the region of fusion breaks down, leaving the contents of the granule outside the cell, and the cell membrane is intact. Ca^{++} ion entry precedes the exocytosis. Most of the hormones, enzymes and neurosecretory substances are secreted in this manner. During this process, the membrane is added to the cell and during endocytosis, the membrane is removed, thus maintaining homeostasis (Figs 4.11A to D).

RECALL Describe the transport of different substances across the cell membranes and their importance.



Figs 4.11A to D: Exocytosis

GIBBS-DONNAN EQUILIBRIUM

The concentration of ions across the membrane is uneven and is maintained under resting conditions.

Consider two chambers containing solutions A and B, separated by a membrane, which is freely permeable to both the cations and anions.

Solution A	Solution B

At equilibrium:

1. Both solutions are neutral, i.e., total number of charges on cations are equal to total charges on the anions. Therefore:

$$\text{Cations in A} = \text{Anions in A} \quad \text{and} \quad \text{Cations in B} = \text{Anion in B} \qquad (1)$$

2. The product of diffusible ions on one side is equal to the products of the diffusible ions on the other side:

$$\text{Diffusible cations in A} \times \text{Diffusible anions in A} = \text{Diffusible cations in B} = \text{Diffusible anions in B}$$

Note: Docking proteins, like 'V' snare protein and 'T' snare protein, participate in exocytosis.

i.e.,

$$\frac{\text{Diffusible cations in A}}{\text{Diffusible cations in B}} = \frac{\text{Diffusible anions in B}}{\text{Diffusible anions in A}} \qquad (2)$$

When a non-diffusible anion is introduced on one side (side A) then the distribution of diffusible ions at equilibrium will be asymmetrical.

Let us consider that K^+, Cl^- are present in both A and B solutions, when a non-diffusible anion, like protein or phosphate is added to the solution 'A.'

Self-Assessment/Review Questions

SHORT ANSWER QUESTIONS

1. Write the functions of the intercellular junctions.
2. What is secondary active transport? Give an example. What is its clinical application?
3. Briefly write about endocytosis, exocytosis and phagocytosis with examples.
4. Name the fluid compartments. Explain the determination of any one of them.
5. What is the ionic composition of ECF and ICF?
6. What is meant by homeostasis? Mention the basic mechanisms that maintain homeostasis with examples.
7. What are the functions of Na-K ATPase?
8. Briefly write about intercellular communication.
9. Differentiate between Resting membrane potential and Action potential.
10. Gap junctions and their functions
11. Active transport
12. Osmosis
13. Endoplasmic reticulum
14. Structure and function of cell membrane
15. Fastening Junctions
16. Co-transport
17. Carrier-mediated transport

LONG ANSWER QUESTIONS

1. What is the principle underlying the measurement of body fluid compartments? Classify the body fluid compartments and give their normal values.
2. A person with severe diarrhea develops dehydration. What is the effect of dehydration on blood pH and other components? How will you manage?
3. Which of the body fluid compartments gets expanded in generalized edema? List any two causes of edema.
4. Explain the reason for generalized edema in hypoproteinemia.
5. Of the two types of edema, intracellular and extracellular, which one is more dangerous? Give your reasons.

CLINICAL CASE-BASED QUESTIONS

1. Mrs Nirmala is a 40-year-old teacher. She was suffering from severe diarrhea for the last 5 days, the stools were watery and copious. She also complained of shortness of breath and fatigue since morning.

Lab report:

1.	Fasting blood sugar	100 mg/dL
2.	pH	7.24
3.	$PaCO_2$	30 mm Hg
4.	Na^+	134n, Eq/L
5.	Cl	106 mEq/L
6.	HCO_3^-	15 mEq/L
7.	K^+	4.2 mEq/L

a. Explain the Lab findings.
b. What is the condition the person is suffering from?
c. What is the cause for your clinical diagnosis?
d. How do you treat this case?
e. What is the effect on her body fluids?
f. What is the effect of this on urine output?

MULTIPLE CHOICE QUESTIONS

1. **Oral rehydration therapy utilizes one of the following mechanisms for rapid restoration of body fluids level:**
   a. Cotransport b. Filtration
   c. Diffusion d. Endocytosis
2. **Gap junctions are present in one of the following tissues:**
   a. Skeletal muscle b. Neurons
   c. Cardiac muscle d. Epithelial tissue
3. **The normal ECF value of a 70 kg person:**
   a. 10 L b. 14 L
   c. 28 L d. 2 L
4. **Resting membrane potential develops mainly due to:**
   a. K^+ efflux b. Cl^- influx
   c. Ca^{++} influx d. Na^+ efflux

ANSWER KEY

1. a **2.** c **3.** b **4.** a

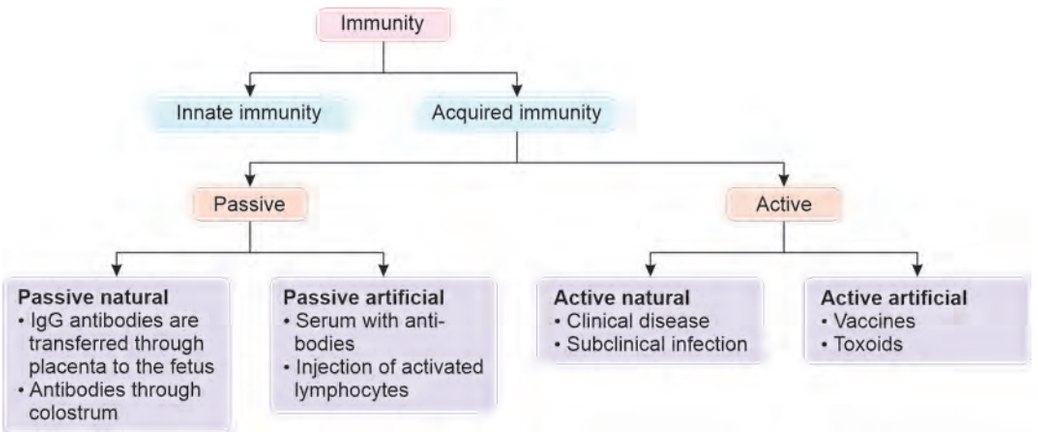


Fig. 56.1: Body immunity mechanisms

INNATE IMMUNITY

This is a non-specific immunity present in all the subjects from birth. It protects the body from all types of disease causing organisms. This includes the following mechanisms:

- **Skin:** It acts as a physical barrier and prevents the invasion of the body by disease-causing organisms. Chemicals present in sweat, sebum and wax have antibacterial activity and help in body defense.
- **Mucous membranes:** These are present in the respiratory, digestive and urogenital systems. The *pH, lysozymes and antibodies* of the mucus prevent invasion by the pathogens by their bacteriostatic and bactericidal effects. The ciliated epithelia of the mucosa and the adhesive properties of the mucus also help in defense.
- **Reflex mechanisms** like sneezing, coughing and vomiting help in body defense by expelling the pathogens.
- **Body secretions:** (i) Saliva, gastric juice and intestinal juice with their specific pH and lysozymes also participate in body defense by destroying the pathogens. Lysozymes break the cell membrane of the bacteria, etc. (ii) Tears also contain lysozymes, which destroy bacteria. (iii) Sebum secreted by skin glands has bactericidal and bacteriostatic effects.
- Normal *urination* and *defecation* prevent the growth of bacteria.
- **Microphages:** Neutrophils and eosinophils have phagocytic activity and destroy the pathogens by phagocytosis.
- **Macrophages:** These cells spread over the entire body. They destroy the invading organisms by phagocytosis.
- **Natural killer cells:** These are a separate class of lymphocytes, which can kill pathogens, tumor cells, viral infected cells by directly attacking them. These are not processed by either the bone marrow or the thymus.
- Some *basic proteins* present in the body fluids do not allow the growth of bacteria and thus participate in body defense.
- **Interferons:** These are released by viral infected cells. These prevent multiplication of viruses.
- **C-reactive protein:** Following an infection, C-reactive protein levels increase in the plasma. These activate complements, which facilitate phagocytosis.
- **Normal GIT flora:** Normal flora present in the GIT does not allow the growth of pathogenic organisms.
- **Complement complexes:** These facilitate phagocytosis of the foreign organisms by acting as opsonins. They may also destroy the cell wall of the bacteria. (Please see the complement system.)

Differences between innate and acquired immunity are tabulated as follows:

Innate immunity	Acquired immunity
• Present from birth	• Acquired during one's lifetime when pathogen enters the body
• Provide non-specific immunity	• Provide immunity against a particular pathogen
• Provide temporary immunity	• Provide permanent immunity
• Skin, mucosa, NK cells, macrophages neutrophils, etc. participate	• Humoral (B-lymphocyte cell mediated immunity, T-lymphocyte participate)

RECALL Differentiate innate from acquired immunity.

1. Complement system, 2. C-reactive protein and 3. Interferons are referred to as *innate humoral immune system*

Neutrophils, eosinophils, NK cells and Monocyte macrophage system are referred to *as innate cell mediated immunity.*

TABLE 68.4: Comparison of the four heart sounds

First heart sound (S1)	Second heart sound (S2)	Third heart sound	Fourth heart sound
• **Cause:** It is produced due to closure of AV valves and marks the beginning of ventricular systole	• **Cause:** It is produced due to closure of semilunar valves and marks the beginning of ventricular diastole	• **Cause:** It is produced by the vibration of the ventricular wall and turbulence of blood flow during 1st rapid filling	• **Cause:** It is produced due to atrial systole during last rapid filling phase of the ventricle
• **Character:** Low-pitched, loud sound with <50 Hz, it sounds like LUBB Phonocardiographic pattern shows 7–13 vibrations	• **Character:** High-pitched, sharp sound with >50 Hz, it sounds like DUP Phonocardiographic pattern shows 4–6 waves	• **Character:** Low pitched sound usually not audible. Phonocardiographic record shows 1–4 waves.	• **Character:** Low pitched sound. Not audible, phonocardiographic record shows 1–2 waves.
• **Type of sound:** It is a continuous audible sound	• **Type of sound:** It is an audible split sound	• **Type of sound:** In 30% of children and young adults it is audible	• **Type of sound:** Completely inaudible
• **Duration:** It lasts for 0.14–0.17 sec	• **Duration:** It lasts for 0.1–0.14 sec	• **Duration:** It lasts for less than 0.1 second	• **Duration:** Its duration is even shorter than 3rd heart sound
• **Site:** It is audible all over the chest. But better audible at tricuspid and mitral areas	• **Site:** It is audible all over the chest but better audible at aortic and pulmonary areas	• **Site:** Can be recorded from all the four areas	• **Site:** Can be recorded from all the four areas
• **Correlation:** It coincides with 'R' wave of ECG, carotid pulse and 'apex beat'	• **Correlation:** It coincides with the end of 'T' wave of ECG - 'v' wave of JVP - IVMC of ventricle	• **Correlation:** It appears during 1st rapid filling phase	• **Correlation:** It appears during 2nd rapid filling phase of the ventricular filling. It coincides with 'a' wave of JVP (atrial systole)

Mechanism of Production

It is caused by the closure of AV valves. In general, three different components are considered in the production of the 1st HS. These are:

1. Valvular
2. Muscular
3. Vascular components

The closure of AV valves causes vibrations of the valve cusps and chordae tendinae. The ventricular myocardium, which is then undergoing isovolumetric contraction also vibrates contributing the muscular component. Vascular component refers to the vibration of the aortic wall as a result of transmission by the ventricular myocardium. *This sound is better heard over the mitral and tricuspid areas.*

Clinical Correlation of S1

- The first heart sound *marks the onset of ventricular systole.*
- It becomes *abnormal in AV valve disease* in particular and disease of heart in general.
- It appears as a *split sound in a bundle branch block.*
- It becomes *louder in LVH, anemia and pregnancy.*

Second Heart Sound (S2)

It is described as DUP. It is a short, sharp and high pitched sound with more than 50 Hz. The duration is 0.1–0.14 sec. Phonocardiographic pattern shows 4–6 waves. It is caused by closure of semilunar valves (aortic and pulmonary valves). *It is heard as a split sound (double) because the aortic valve closes earlier than the pulmonary valve.* So the 2nd sound has aortic and pulmonary components separated by a small interval. This interval is *more in inspiration* and *less in expiration. In the case of an atrial septal defect, the split becomes constant. This sound is better heard at the pulmonary and aortic areas.* The aortic component is better audible at aortic area and pulmonary component at pulmonary area. It coincides with end of 'T' wave of ECG.

Clinical Correlation of S2

- It indicates the end of ventricular systole.
- Splitting of the 2nd sound is the useful guide in the diagnosis of an atrial septal defect, where the split becomes wider and fixed.
- In RBBB and pulmonary stenosis, split becomes wider.
- Aortic component becomes louder in systemic hypertension and the pulmonary component becomes louder in pulmonary hypertension.

Third Heart Sound (S3)

A low-pitched sound that can be *heard by stethoscope in 30% of children and young people under normal CV conditions.* It is heard in adults in certain pathological conditions.

LPR Fundamentals of Medical Physiology

Salient Features

- This 8th edition of LPR's Fundamentals of Medical Physiology is duly updated with all the latest concepts of physiology.
- It is based on the requirements of Competency-Based Medical Education (CBME) curriculum which are mentioned and marked along with the topics.
- Each and every chapter has been designed in a manner to facilitate better learning and easy retention of the concepts.
- Each chapter starts with competency numbers which are categorized as must know topics for the students.
- Clinical correlation of a topic connects to clinical situation, and its physiological bases are added.
- Recent concepts are simplified, added and are made student friendly for quick learning.
- Applied physiology topics and clinical case scenarios are added as per the requirement of the latest curriculum.
- 1500+ colorful hand-drawn figures and images relevant to the topics are added liberally to make the content more student friendly.
- Complex and difficult topics have been supplemented with numerous tables and flowcharts for easy and quick understanding.
- Self-assessment review exercises with a variety of questions, like Short Notes, Clinical Questions, Multiple Choice Questions have been added for assessing the preparation after completing the respective section.
- Thought-provoking questions along with flowing matter help the student for instant recollection of the relevant points as Recall Box.
- Newly-added content in the book as per the CBME-2019:

  (See Under Section I: General Physiology)
  - **Chapter 1:** Introduction to Physiology [Containing Scientists' Contributions to Physiology](Vol. 1)

  (See Under Section XIV: Integrated Physiology)
  - **Chapter 12:** Cytological Methods and their Applications in Clinical Care and Research (Vol. 2)
  - **Chapter 13:** COVID-19 (Vol. 2)
  - **Chapter 14:** Acquired Human Immunodeficiency Syndrome (Vol. 2)
  - **Appendix I:** Clinical Case Scenario and Solution
  - **Appendix II:** Numerical Formulas for Quick Review
  - **Appendix III:** Physiological Problems and Solutions
- Newly-added topics, like Criterion for Brain Death Confirmation, Gut-Brain Axis, Gut-Brain-Heart Axis, Pregnancy-Psychological-Psychiatric Disorders, Psychological and Psychosocial Changes Associated with Puberty and many more enrich the content.

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Dr Reddy is an eminent scholar and has to his credit more than 20 national and international professional publications. He runs a YouTube Channel "LPR Physiology Fundamentals-YouTube", where he teaches the concepts of Physiology to students. He has authored books on Physiology, viz. LPR Fundamentals in Medical Physiology, Human Physiology for Dental Students, Practical Physiology for Medical Students, and LPR's MCQs in Medical Physiology.

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Eighth Edition

Volume 2

LPR Fundamentals of Medical Physiology

As per the Competency-Based Medical Education Curriculum (NMC) for the Indian Medical Graduates

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L Prakasam Reddy

Volume
2

LPR Fundamentals of Medical Physiology

As per the Competency-Based Medical Education Curriculum (NMC) for the Indian Medical Graduates

Eighth Edition

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Contributors

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Vidya Reddy
L Dhanalakshmi
Naren Prakash Reddy

PREFACE TO THE EIGHTH EDITION

It is a pleasure to bring out the eighth edition of ***LPR Fundamentals of Medical Physiology*** in a completely revised and student-friendly format. This edition has been thoroughly updated based on the latest Competency-Based Medical Education (CBME) curriculum. The entire subject of Physiology is divided into competencies and sub-competencies. Scenario-based and task-based questions are given at the end of each section to enable the students to do the self-assessment test and appear confidently for the exams.

What is Competency?

Competency is defined as "the ability to do something successfully and efficiently." CBME is an approach to ensure that the graduates develop the competencies required to fulfill the patients' needs in the society. Teaching of Physiology to the medical graduates is as per the CBME-2019.

I. Goal

The broad goal of the teaching of undergraduate students in physiology is to provide the student with comprehensive knowledge of the normal functions of the organ systems of the body to facilitate an understand the physiological basis of health and disease.

II. Objectives

A. **Knowledge:** At the end of the course the student will be able to:
   1. Explain the normal functioning of all organ systems and their interactions for well-coordinated total body functioning.
   2. Assess the relative contribution of each organ system to the maintenance of the milieu interior.
   3. Elucidate the physiological aspects of normal growth and development.
   4. Describe the physiological response and adaptations to environmental stress.
   5. List the physiological principles underlying pathogenesis and treatment of the disease.

B. **Skills:** At the end of the course the student will be able to:
   1. Conduct experiments designed for study of physiological phenomenon.
   2. Interpret experimental/investigative data.
   3. Distinguish between normal and abnormal data derived as a result of the tests which he/she has performed and observed in the laboratory.

C. **Attitude and communication skills:** At the end of the course the student will be able to:
   1. Show due respect to the persons who volunteer to be examined for the purpose of learning clinical examination.
   2. Communicate effectively with peers and teachers.
   3. Demonstrate the ability of team work.

D. **Integration:** At the end of the first year integrated teaching, the student should acquire an integrated knowledge of organ structure and function and the regulatory mechanisms and tests to assess the functional status of organ systems.

The student should know the basic features of clinical conditions explained at the end of each chapter. This helps the student in getting ready with the clinical knowledge before he/she enters the portals of hospital.

L Prakasam Reddy

83 Functional Anatomy of Gastrointestinal Tract

COMPETENCY

Competency achieved after reading this chapter:

PY4.1 - Describe the structure and functions of digestive system.

Horizontal Integration-Anatomy

CHAPTER OUTLINE

- Parts of Human Digestive Canal
- Functions of Alimentary Canal
- General Structure of Alimentary Canal
- Nerve Supply
- General Regulatory Mechanisms of GIT Secretions

PARTS OF HUMAN DIGESTIVE CANAL

The human digestive canal is a long muscular tube (Fig. 83.1) consisting of the following parts:

Mouth: It is the first part of gastrointestinal tract (GIT) that helps in ingestion and chewing of food. Saliva is poured into the mouth by salivary glands.

Pharynx: This is a junction where seven channels open. Two posterior nares, two pharyngo-tympanic tubes, oral cavity, esophagus and larynx all meet at pharynx. Around this, lymph nodes are arranged in a ring-like manner. Air is directed into the trachea. Food is directed into the esophagus.

Esophagus: It is a fibro-muscular tube lined with mucus membrane. It is about 25 cm long and propels food into the stomach.

Stomach: It is a muscular bag that receives and stores food. Food is converted into chyme and then fed into duodenum.

Duodenum: The first part of small intestine. Pancreatic juice and bile enter duodenum during digestion.

Jejunum: It is the continuation of duodenum and continues down as ileum.

Ileum: It is the continuation of jejunum. Digestion and absorption take place mainly in these three divisions. A valve called *ileocecal valve* is present at opening of ileum into the cecum.

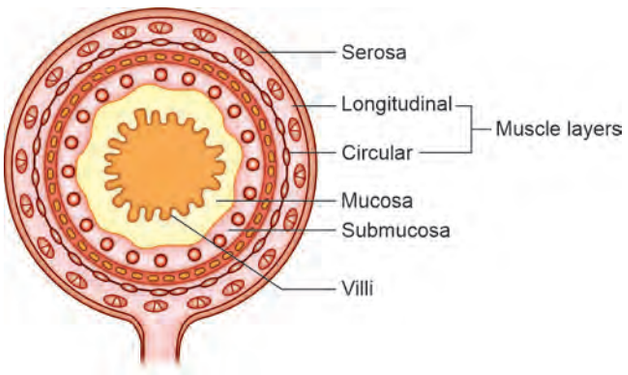

Fig. 83.2: Transverse section of the small intestine

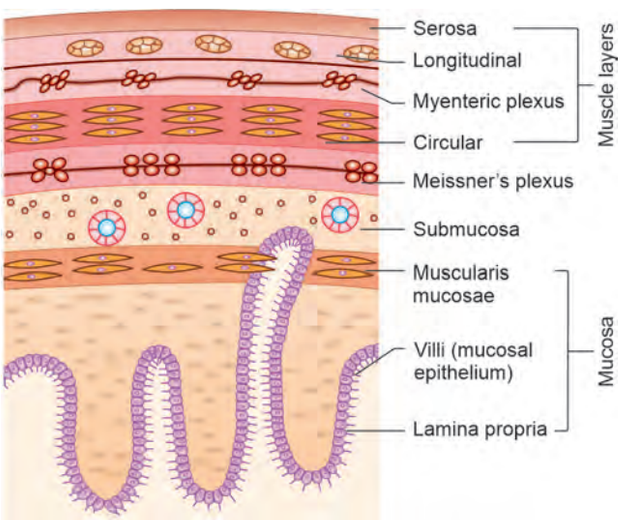

Fig. 83.3: A section of the duodenum enlarged

villi, which are lined by columnar epithelial cells. The epithelial cells give rise to hair-like processes called *microvilli*. This arrangement increases the surface area (Figs 83.2 and 83.3).

This has a role in the absorption of digested foods and secretions.

NERVE SUPPLY

- Extrinsic nerve supply
- Intrinsic nerve supply

Extrinsic Nerve Supply

This comprises both the divisions of autonomic nervous system that supply the alimentary canal and higher centers (Figs 83.4 and 83.5).

Higher centers: The higher centers that influence GIT are cerebral cortex, limbic system and hypothalamus. These

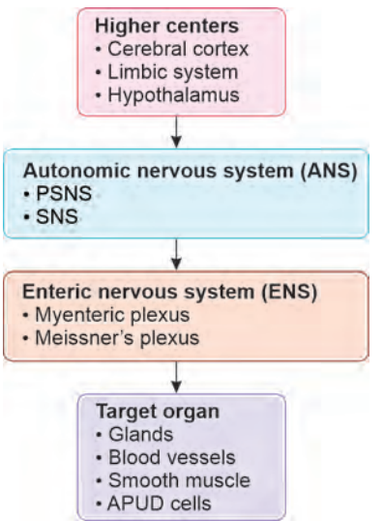

Fig. 83.4: Nerve supply to GIT

higher centers influence GIT function through autonomic nervous system. They may have either inhibitory or facilitatory influence on: (i) *motility* and (ii) *secretions*.

Autonomic nervous system: *Sympathetic Nervous System (T6-L2 Spinal Segments):* The sympathetic nerve fibers to the GIT are supplied through *splanchnic and presacral nerves.* Both efferent and afferent fibers are present. The afferents are concerned with the transmission of pain to the higher centers. The efferents release norepinephrine and bring about both excitatory and inhibitory effects through *alpha* and *beta receptors.* Thus sympathetic activation causes:

- Decrease in GIT motility.
- Decreased blood flow by causing vasoconstriction.
- Decreased secretions indirectly by decreasing blood flow.
- Increased activity of sphincters and villi.

The inhibitory effect is mediated through both *alpha* and *beta* receptors, whereas excitatory effect is mediated only through *alpha* receptors.

Parasympathetic nervous system: The vagus *(10^{th} cranial nerve)* and pelvic nerves *(S2, 3, 4 sacral)* supply to the GIT including glands. Vagus supplies from the esophagus to the transverse colon and pelvic nerves supply to the rest of the large intestine. Parasympathetic nerves contain both afferent and efferent fibers.

- The afferents detect the distension of the gut, chemical composition and osmolality of the chyme.
- The efferent parasympathetic nerve fibers release acetylcholine which acts through M_3 *receptors.* Thus, activation of parasympathetic nerves causes:
  - Increase in motility of GIT
  - Relaxation of the sphincters
  - Increase in GIT secretions

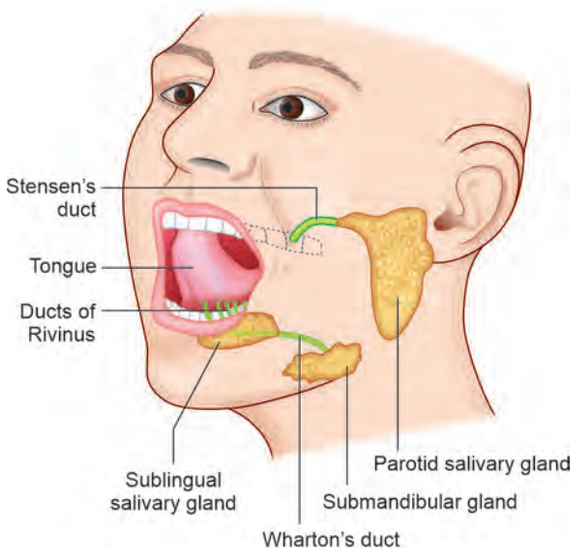

Fig. 84.1: Location of salivary glands and their ducts

Additional Glands

- Lingual
- Labial
- Buccal
- Palatine glands

These contribute 5% to the saliva.

Location

Parotid gland: Largest; weight: 20–30 g; and is *present in the side of the face below the ear* and in front of it. Secretions are passed on to the mouth by *Stensen's duct*, which opens into the oral cavity opposite to the upper second molar teeth. Contributes 20% of total saliva.

Submandibular: Weight: 8–10 g; and is *present in the submaxillary triangle* on the inner side of the lower jaw. *Wharton's duct* carries the secretions into the mouth and opens on the summit of the papilla, known as *caruncula sublingualis.* It is located on the side of the frenulum of the tongue. Contributes 70% to total saliva.

Sublingual gland: It is the smallest of the salivary glands. *Weight 2–3 g and is present under the mucus membrane on the floor of the mouth.* Contributes 5% to total saliva.

Secretions are carried by means of 15–20 ducts, called *ducts of Rivinus,* which open through the floor of the mouth. Sometimes, the anterior portion of the gland is drained by a single large duct called *Bartholin's duct.*

Structure

Presents a *racemose structure,* which consists of *acini* and *the duct system* (Fig. 84.2). *Acinus* is the secretory unit of the salivary gland and is *also known as alveolus.* Acinus consists of:

- Secretory epithelial cells are arranged around the central lumen. The epithelial cells are pyramid-shaped cells, resting on a definite basement membrane.
- Between the epithelial cells and the basement membrane, there are special types of cells called *basket cells (myoepithelial cells).* These are contractile in nature and aid in the expulsion of saliva to the central lumen.
- Duct cells extend into the lumen of the acinus called *centroacinar cells.*

Depending on the secretion and histological appearances, there are two types of acini. These are: 1. *Serous acini,* 2. *Mucus acini (Fig. 84.3).*

Serous acini: Secrete thin watery saliva rich in enzymes.

Mucus acini: Secrete thick viscous saliva rich in mucin content.

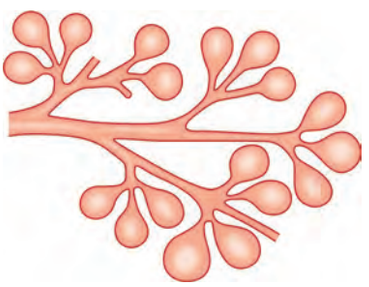

Fig. 84.2: Racemose pattern of salivary gland

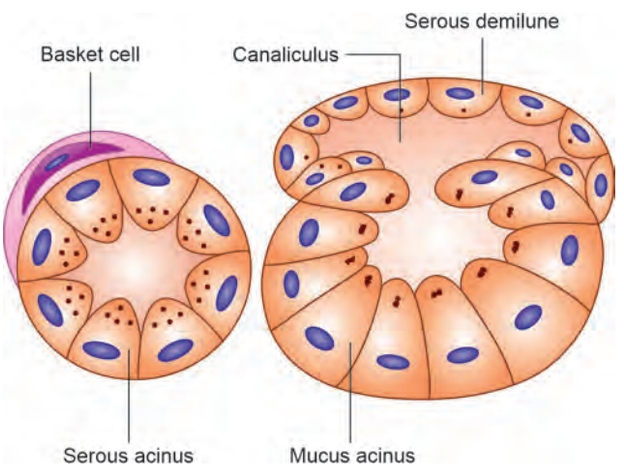

Fig. 84.3: Types of acini in a salivary gland

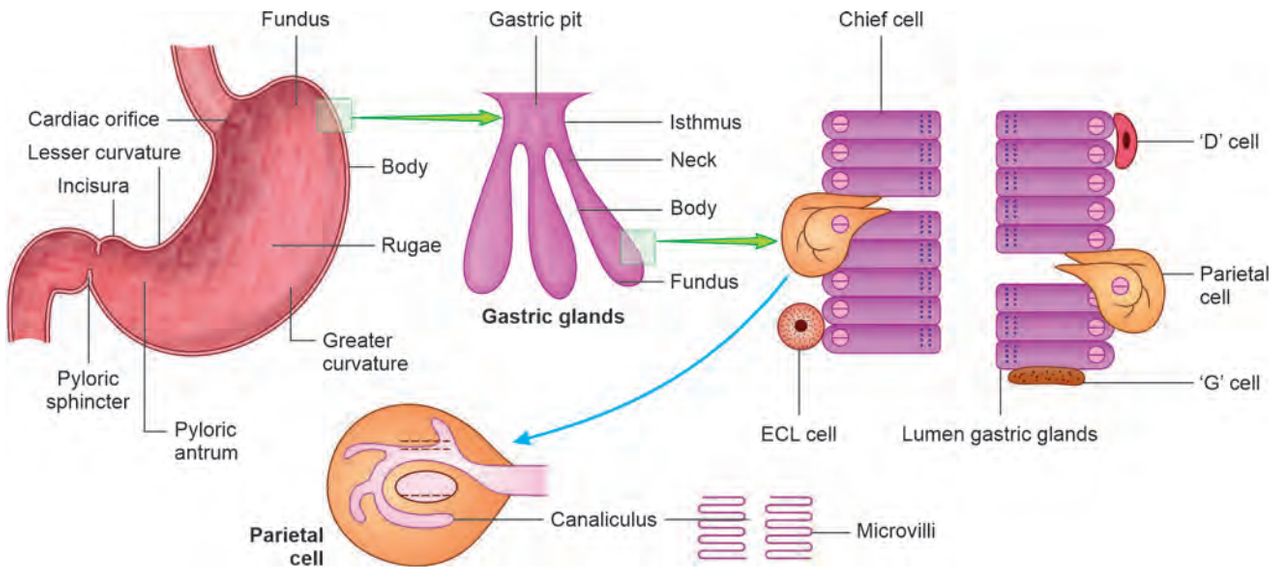

Fig. 85.1: Structure of stomach

Submucosal layer: It is the connective tissue containing lymphatic blood vessels and nerves. Meissner's plexus is present between the muscular and submucosal layers.

Mucosal layer: The mucus membrane is thrown into folds when the stomach is empty. *These folds are called rugae.* These *disappear when the stomach is full.* On the surface of the mucosa there are numerous minute openings called *gastric pits. Three to seven gastric glands open into each gastric pit.* The *surface* of the mucus membrane is always covered by a thick *layer of the mucus, secreted by the surface epithelial cells.* This mucus with a thickness of *0.5–2.5 mm protects the mucosa* from the *injurious effects of gastric HCl.* The surface epithelial cells of gastric mucus membrane are continuously shed, but are replaced by new cells. The new cells come from the cells present at the base of gastric pits. The entire gastric mucosa is divided into:

- **Cardiac area:** 1.5 cm in width around the cardiac orifice
- **Fundic area:** 60–80%
- **Pyloric area:** 15–20%

GASTRIC GLANDS (PY4.2)

The shape and structure of gastric glands vary in different parts of the stomach. In the fundus and the body, the glands are long and straight. But in the pylorus and in the cardiac area the glands are short and tortuous (Fig. 85.2).

Types of Gastric Glands

Three types of gastric glands are identified:

1. **Oxyntic glands:** These are present in the fundus and the body. All four types of cells are present and produce both acid and enzymes.
2. **Cardiac glands:** These are present in the cardiac area. Mainly mucus cells, but a few chief cells. These produce a soluble mucin and enzymes.
3. **Pyloric glands:** These contain mucus cells, which produce mucin only. The surface of the mucosa of pyloric antrum contains *'G'* cells, which produce gastrin.

   Each gland has the following parts:
   - Mouth
   - Isthmus
   - Neck
   - Body
   - Fundus

Cells of Gastric Glands

Six different types of cells are present in the gastric glands (Fig. 85.1). These cells are:

1. *Chief cells* or zymogen cells - Pepsinogen
2. *Parietal cells* or *oxyntic cells* - HCl and Intrinsic factor.
3. *Mucus cells* - Soluble mucin
4. *ECL or Enterochromaffin - like cells*- Histamine
5. *'D' cells* - Somatostatin
6. *'G' cells* - Gastrin

Chief cells or Zymogen cells

- Distributed throughout the gastric gland, except a small area at the neck of the gland.
- They are columnar in shape.
- Nucleus (round) located toward the base of the cells.
- Zymogen granules present in cytoplasm close to the lumen of the gland so that secretions can be poured into the lumen directly.

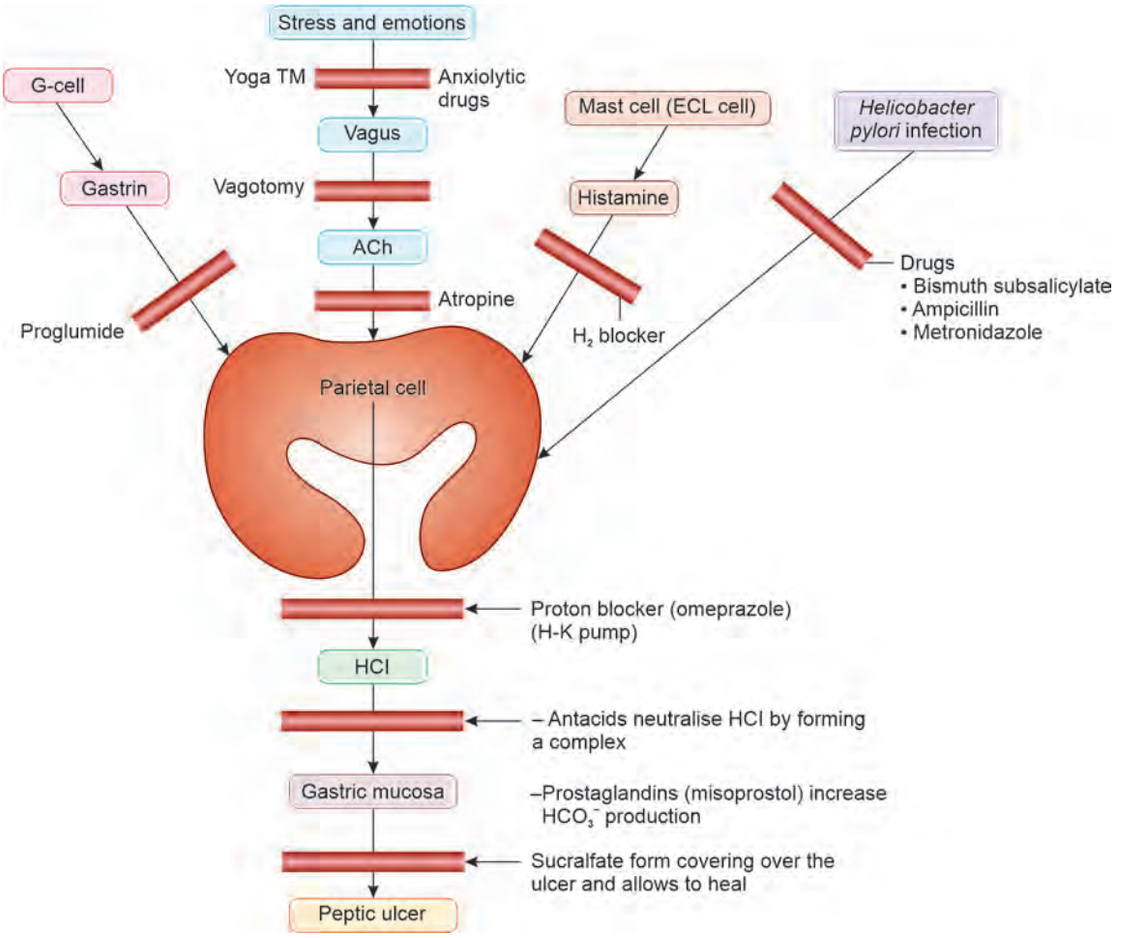

Fig. 85.13: Physiological principles in the treatment of hyperacidity and peptic ulcers

Abbreviation: TM, transcendental meditation

Estimation of serum gastrin levels
Normal Fasting Level of Gastrin is 20–150 pg/mL

Applied Physiology

Effect of Total Gastrectomy

It means complete removal of stomach by surgery. The following features may develop:

- *Pernicious anemia* develops due to deficiency of intrinsic factor.
- Since bacteria are not killed there is a *chance for infection.*
- HCl releases iron from foods and converts Fe^{++} to Fe^{+++}. As HCl is absent this may predispose to *iron deficiency anemia.*
- Rapid absorption of glucose leads to hyperglycemia, which in turn causes *hypoglycemia 2 hours after food intake through insulin release.*
- *Protein digestion is not affected.*
- *Dumping syndrome may develop - See Dumping syndrome.*
- *Dimorphic anemia (hypochromic-macrocytic anemia)*

Achlorohydria

True: *No acid secretion even after the stimulus is applied.* This is associated with pernicious anemia, myxedema, gastritis, iron deficiency anemia, carcinoma of stomach, etc.

Apparent: *There is acid secretion after the stimulus application.*

Contd...

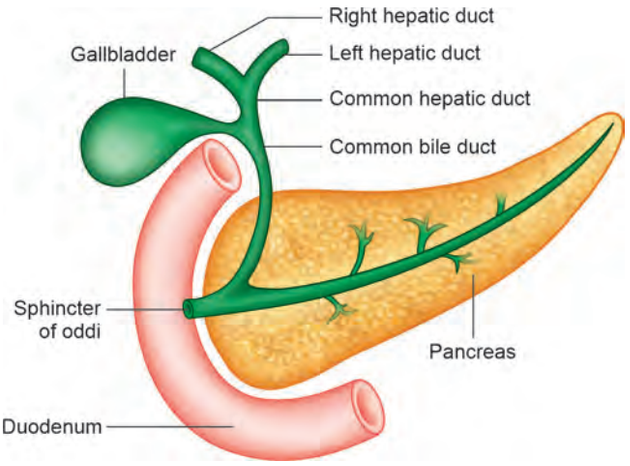

Fig. 86.1: Drainage of bile and pancreatic juice into the duodenum

The endocrine part produces *insulin, Amylin, glucagon, PP and somatostatin.* Exocrine part produces *enzymes, HCO_3^- and water.*

Microscopic Structure of Exocrine Pancreas

Pancreas presents a compound racemose structure. The secretory unit of the exocrine portion is the acinus. The acini join together to form a primary lobule. Number of primary lobules join together to form a secondary lobule.

Each acinus is lined by secretory epithelial cells. The shape of these cells is oval, cuboidal, polyhedral, etc. These cells arrange around a central lumen. The cells contain rounded nucleus at the base and apical granules in the cytoplasm. These granules are zymogen granules and they represent precursors of pancreatic enzymes. Acinar cells secrete enzymes, electrolytes, HCO_3^- and H_2O. Central lumen opens into intercalated ducts. These join together to form intralobular ducts. The ducts in turn join to form interlobular ducts. Ducts are lined by cuboidal epithelium. Cuboidal lining of the intercalated ducts extends into the lumen of the acinus. These cells are known as centroacinar cells (Fig. 86.2).

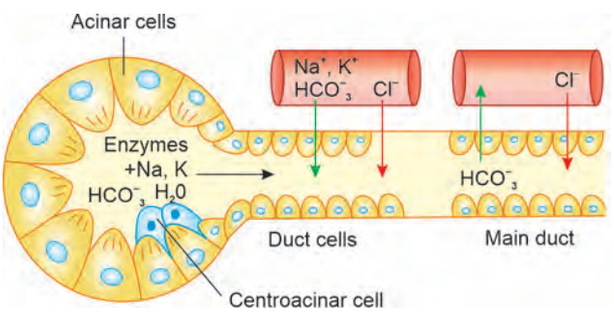

Fig. 86.2: Mechanism of secretion of pancreatic juice

PANCREATIC JUICE (PY4.2)

Source of Pancreatic Juice

Acinar cells secrete enzymes, electrolytes, HCO_3 and H_2O. Centroacinar cells, intercalated ducts, intralobular ducts and interlobular ducts secrete electrolytes and H_2O. In the main ducts, Cl^-—HCO_3^- exchange takes place.

Nerve Supply

Supplied by *vagus* (parasympathetic) and splanchnic nerves (sympathetic). Vagus stimulates enzyme-rich pancreatic juice. *Sympathetic nerves* mainly decrease blood flow by their vasoconstrictor effect.

Composition

- It is a colorless, odorless watery secretion isosmotic with that of plasma.
- About 1–1.5 liters of pancreatic juice is secreted in 24 hours.
- It is secreted throughout the day. Initially, its secretion is low and *reaches peak by 2–3 hours after food intake* and again declines and reaches basal level during interdigestive phase (Fig. 86.3).

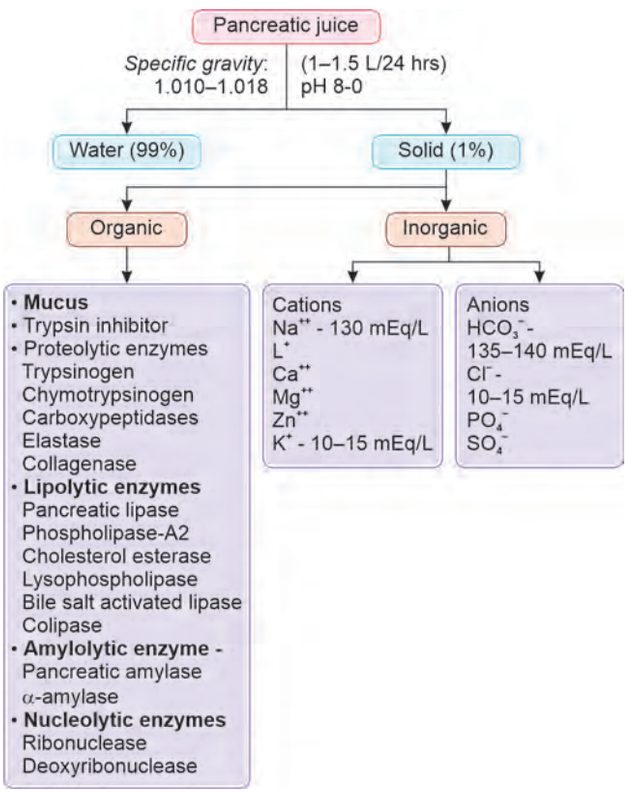

Fig. 86.3: Composition of pancreatic juice

Note:
HCO_3^- concentration increases with increased rate of secretion.
Cl^- concentration is inversely related to HCO_3^- concentration.
Its concentration decreases with increase in secretion.

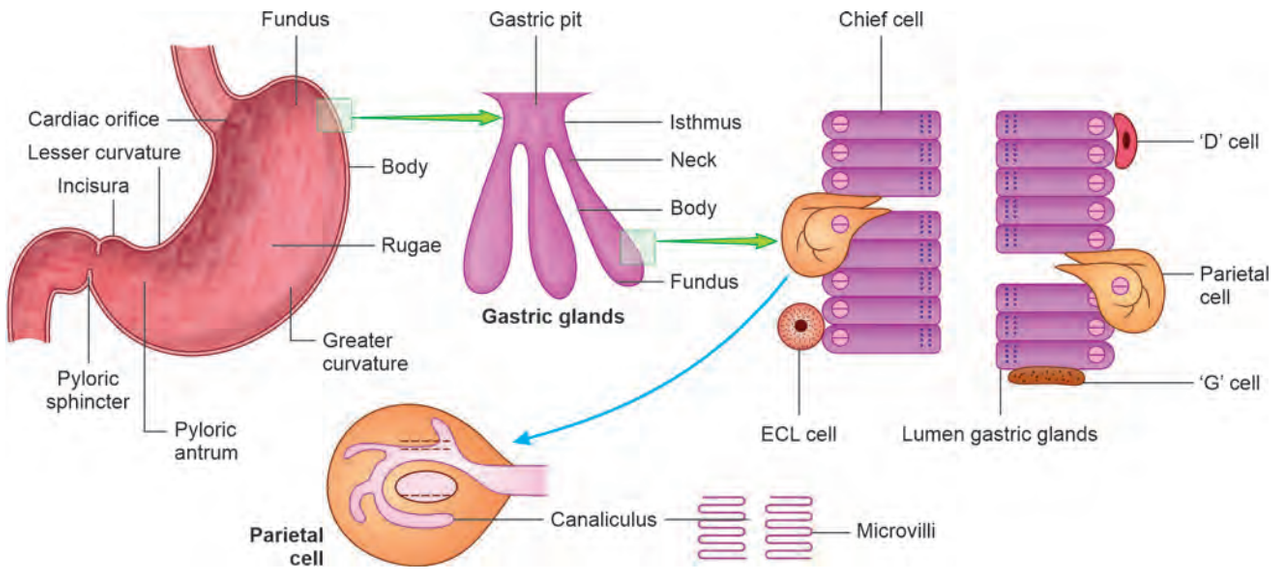

Fig. 85.1: Structure of stomach

Submucosal layer: It is the connective tissue containing lymphatic blood vessels and nerves. Meissner's plexus is present between the muscular and submucosal layers.

Mucosal layer: The mucus membrane is thrown into folds when the stomach is empty. *These folds are called rugae.* These *disappear when the stomach is full.* On the surface of the mucosa there are numerous minute openings called *gastric pits. Three to seven gastric glands open into each gastric pit.* The *surface* of the mucus membrane is always covered by a thick *layer of the mucus, secreted by the surface epithelial cells.* This mucus with a thickness of *0.5–2.5 mm protects the mucosa* from the *injurious effects of gastric HCl.* The surface epithelial cells of gastric mucus membrane are continuously shed, but are replaced by new cells. The new cells come from the cells present at the base of gastric pits. The entire gastric mucosa is divided into:

- **Cardiac area:** 1.5 cm in width around the cardiac orifice
- **Fundic area:** 60–80%
- **Pyloric area:** 15–20%

GASTRIC GLANDS (PY4.2)

The shape and structure of gastric glands vary in different parts of the stomach. In the fundus and the body, the glands are long and straight. But in the pylorus and in the cardiac area the glands are short and tortuous (Fig. 85.2).

Types of Gastric Glands

Three types of gastric glands are identified:

1. **Oxyntic glands:** These are present in the fundus and the body. All four types of cells are present and produce both acid and enzymes.
2. **Cardiac glands:** These are present in the cardiac area. Mainly mucus cells, but a few chief cells. These produce a soluble mucin and enzymes.
3. **Pyloric glands:** These contain mucus cells, which produce mucin only. The surface of the mucosa of pyloric antrum contains *'G'* cells, which produce gastrin.

   Each gland has the following parts:
   - Mouth
   - Isthmus
   - Neck
   - Body
   - Fundus

Cells of Gastric Glands

Six different types of cells are present in the gastric glands (Fig. 85.1). These cells are:

1. *Chief cells* or zymogen cells - Pepsinogen
2. *Parietal cells* or *oxyntic cells* - HCl and Intrinsic factor.
3. *Mucus cells* - Soluble mucin
4. *ECL or Enterochromaffin - like cells*- Histamine
5. *'D' cells* - Somatostatin
6. *'G' cells* - Gastrin

Chief cells or Zymogen cells

- Distributed throughout the gastric gland, except a small area at the neck of the gland.
- They are columnar in shape.
- Nucleus (round) located toward the base of the cells.
- Zymogen granules present in cytoplasm close to the lumen of the gland so that secretions can be poured into the lumen directly.

Other Factors

Neural:

- Parasympathetic fibers through the vagus increase gastric peristalsis and emptying.
- Sympathetic nerve fibers decrease gastric peristalsis and emptying.

Hormonal:

- *Gastrin* facilitates gastric emptying.
- Pentagastrin, CCK-PZ, secretin, VIP, GIP, somatostatin and bombesin inhibit gastric emptying.

Applied Physiology

Vomiting (Emesis) (PY4.9)

Vomiting is a reflex act by which the upper GIT is relieved of its contents through the mouth. It is a complicated reflex, which can be initiated by stimulating vomiting center. Vomiting center can be activated *either directly* or *through Chemo Trigger Zone (CTZ).*

Direct activation of vomiting center: Vomiting center can be activated either directly or through afferent impulses coming from the different parts of the body. Vomiting center is located in the reticular formation of medulla near nucleus tractus solitarius.

- Increase in intracranial pressure, meningitis stimulate vomiting center directly and cause a rapid forceful emesis called *projectile vomiting*
- Afferents from visceral organs
- Metabolic disturbances

Afferent impulses from visceral organs of body: Afferents from upper GIT kidney, heart, uterus and urinary tract travel through autonomic nerve fibers, stimulate vomiting center. Tickling of back of throat, distension of stomach, injury to the urinary tract cause vomiting.

Metabolic disturbance in pregnancy: It is mostly due to carbohydrate starvation and ketosis.

Activation of CTZ (Indirect activation of VC): CTZ is located in the *area postrema* and is outside the blood brain barrier. This is stimulated by the following factors.

- Abnormal stimulation of vestibular apparatus as in the case of motion sickness.
- Radiation
- Some drugs called emetics such as apomorphine, emetine, picrotoxin and digitalis.
- Visual input, limbic input and cortical input.

Efferents from vomiting center: The *motor impulses* causing the act of vomiting are transmitted from vomiting center through *V, VII, IX, X and XII cranial nerves* to the upper part of GIT and *through spinal nerves* to *diaphragm and abdominal muscles.*

Mechanism of vomiting (sequence of events)

Stage I: *Vomiting always follows or begins with nausea.* Nausea is characterized by hyper salivation along with some disagreeable sensations. *Pallor, sweating and tachycardia also appear along with nausea* (Fig. 91.6).

Stage II: During nausea antiperistalsis begins in ileum, which propels the small intestinal contents into the stomach. Pyloric sphincter and pyloric antrum contract, pushing the contents into the body and fundus, which are relaxed and dilated.

Stage III: After an inspiratory effort, glottis is closed and respiration is arrested. Abdominal muscles contract in a jerky manner compressing the stomach between the contracted diaphragm and the abdominal viscera.

Note: The initial sequence of events can occur repeatedly without expulsion via the mouth and is known as retching.

Contd...

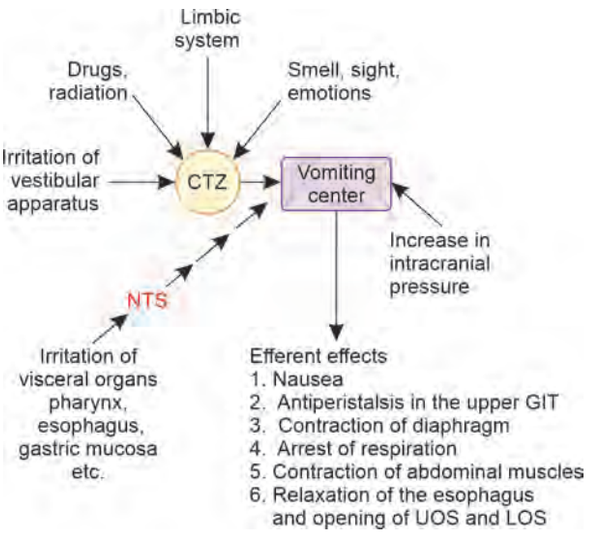

Fig. 91.6: Neural mechanisms in vomiting reflex

The lower esophageal sphincter, esophagus and upper esophageal sphincter relax. The stomach contents are ejected out through relaxed esophagus and mouth due to high pressure in the stomach. During the ejection of vomitus, glottis is closed, respiration is arrested and so vomitus does not enter larynx. The entry of vomitus into the nasopharynx is prevented by the elevated soft palate.

Emetics: These are chemicals that induce vomiting.

Antiemetics: These are chemicals that prevent vomiting.

Effects of persisting vomiting: In gastritis or increased intracranial pressure, meningitis or due to other stimuli, vomiting center is stimulated causing persisting vomiting.

- There is a *loss of fluid and electrolytes along with acid.*
- *Metabolic alkalosis develops.*
- As fluid is lost, there may be *hypovolemia with electrolyte disturbances.*
- Food intake is reduced, leading to weight loss and nutritional disturbances. Body fluid level may become less leading to *dehydration.*

Dumping Syndrome

Patients with *gastrojejunostomy* or with *gastrectomy* carried out for healing of duodenal ulcers *develop some symptoms, which are collectively called dumping syndrome.*

Symptoms: These include *weakness, dizziness* and *sweating,* which *appear about 2 hours after meals.* These symptoms may be due to:

- **Hypoglycemia:** Glucose is rapidly absorbed which stimulates insulin secretion, which in turn, causes hypoglycemia.
- **Hypovolemia:** It may be due to reduction in plasma volume, thereby decreasing cardiac output and a fall in BP.
  Rapid entry of hypertonic meals into the intestine provokes the movement of large quantity of water into the gut. This causes a fall in the plasma volume and hypotension leading to weakness, dizziness and sweating.
- **Stimulation of autonomic reflexes** secondary to distension of the small intestine and release of hormones from the gut due to rapid entry of gastric contents into the duodenum and the jejunum may also be responsible for the weakness and dizziness.

Pyloric Stenosis

In some individuals, the pyloric opening into the duodenum becomes narrow due to various reasons. As a result:

- **Gastric emptying** becomes *slow* and *delayed.*
- The subject may develop *gastric ulcers* due to presence of acid in the stomach for longer periods.
- *Digestion* and absorption *delayed.*

ILEOCECAL VALVE

A valve and sphincter-like arrangement is present at the junction of the ileum and the cecum. This is called ileocecal sphincter. This is tonically contracted and remains closed most of the time and prevents reentry of colonic contents into the ileum. Gastrin and gastro-ileal reflex relaxes the ileocecal sphincter and facilitate passage of food residue into the cecum.

Functions

- It allows the passage of intestinal contents after digestion and absorption into the caecum.
- It prevents regurgitation of colon contents into the ileum. The valve can resist reverse pressure of as much as 50–60 cm water.

Gastroileal Reflex

Presence of food in the stomach increases gut motility and gastrin secretion, which causes relaxation of the ileocecal valve. This is called *gastroileal reflex.* The peristaltic waves are responsible for the periodic opening of ileocecal valve. This *facilitates* the *passage of food residue from the ileum into the colon.*

Note: The abdominal tuberculosis commonly occurs at the ileocecal region.

Paralytic Ileus – Adynamic Ileus (PY4.9)

Whenever there is injury to the intestines either due to surgery or due to infection, peritoneal irritation develops, which by reflex mechanism inhibits intestinal movements. This is referred to as paralytic ileus or adynamic ileus. This is due to intestino-intestinal reflex. The peristalsis *reappears* in the small intestine *within 6–8 hours* followed by the appearance of peristalsis in the stomach and *in the colon it takes 2–3 days.*

Mass Peristalsis

Mass peristalsis is seen in large intestine.

GUT-BRAIN AXIS (PY4.6)

The communication system between the gut and brain is called gut-brain axis. It is a biochemical signaling that occurs between the GIT and the brain. The gut-brain axis (GBA) consists of directional communication between the brain and the enteric nervous system linking emotional and cognitive centers of the brain with peripheral intestinal functions. Thus there exists a clear communication between the gut and the brain.

How the Gut and Brain are Connected

The gut and brain are connected both physically and biochemically in a number of different ways. Brain contain 86 billion neurons and the gut contains 100 million neurons. The gut neurons collectively referred to as *enteric nervous system (ENS)* also called *little brain.*

Gut and brain influence reciprocally by three ways:

1. Neural (autonomic nervous system) influence
2. Hormonal influence
3. Chemical influence (Various chemicals released by the gut mucosa and normal gut microbes).

Neural Influence

Autonomic nervous system comprising vagus and sympathetic nervous system connect the gut with the brain reciprocally and exhibit mutual influence. Feeling, moods, fear, anxiety and emotions are influenced by the gut activities, like digestion, motility and absorption from the gut and vice versa. These effects are influenced by some chemicals called *neurotransmitters* which include:

- ACh
- Norepinephrine
- Dopamine
- Serotonin and
- GABA

Emotional and cognitive centers of brain are linked with ENS reciprocally and affect the gut-brain axis. Brain affects the gut function. Emotions, anger, anxiety, sadness, elation, etc. can all trigger symptoms in the gut.

Hormonal influence

Hormones are produced by the brain (Hypothalamus and pineal body). These influence the gut function. Similarly, various hormones produced by gut affect the brain functions, like food intake, emotions, fear, anxiety, digestion motility and absorption.

Chemicals influence

Various chemicals produced by brain (neuropeptides like enkephalins, endorphins, substance P, etc.) influence gut function. Chemicals that are produced by gut (serotonin, bradykinin, PGs, Histamine interleukins, etc.) influence the brain. Nutrients, like short chain fatty acids, vitamins, lipopolysaccharide (LPS) which get absorbed also influence the brain function.

Probiotics: Probiotics are normal gut bacteria that impart health benefits, if consumed. Some of them affect the brain function and are called *"Psychobiotics"*. Symptoms of stress, anxiety and depression are relieved to some extent with ingestion of probiotics. Probiotics show some promise in keeping the *vaginal microbiome in balance as well as treating infections.* These give some hope that their use would enhance brain health.

The gut bacteria affect emotions and the way the brain processes information from the senses like sight, sound flavor or texture.

MULTIPLE CHOICE QUESTIONS

1. An important starch digesting enzyme in the saliva is:
a. Lipase b. Alpha-amylase
c. Trypsin d. Elastase

2. Paralytic salivary secretion is due to increase in sensitivity of the acinar cells to:
a. Catecholamines b. ACh
c. Serotonin d. Dopamine

3. Gastrin is secreted by:
a. G cells b. PP cells
c. S cells d. D cells

4. During deglutition primary peristaltic wave is initiated by:
a. Contraction of soft palate
b. Contraction of superior pharyngeal constriction\
c. Cricopharyngeus
d. Tongue muscles

5. Pancreatic HCO_3^- secretion is mainly stimulated by:
a. CCK-PZ b. Secretin
c. Gastrin d. VIP

6. MMC is seen during one of the following phases:
a. Cephalic phase
c. Interdigestive phase
b. Intestinal phase
d. Digestive phase

7. Defecation reflex in infants is initiated by:
a. Gastroileal reflex
b. Increased CCK levels
c. Increased gastrin levels
d. Gastrocolic reflex

8. Vitamin B_{12} is absorbed from ileum and requires for its absorption:
a. GH b. TSH
c. Intrinsic factor d. Insulin

9. Type of anemia associated with blind loop syndrome:
a. Macrocytic anemia
b. Microcytic anemia
c. Hypochromic anemia
d. Normochromic anemia

10. The effect of histamine on gastric secretion is mediated through:
a. H_1 receptors b. H_2 receptors
c. M_1 receptors d. N receptors

11. Basal electrical rhythm (BER) is generated in GIT by:
a. Longitudinal muscle
b. Circular muscle
c. Myenteric plexus
d. Interstitial cells of Cajal

12. The symptoms of dumping syndrome are caused in part by:
a. Increased blood pressure
b. Hypoglycemia
c. Increased secretion of gastrin
d. Hyperglycemia

13. MMC is initiated during interdigestive phase by:
a. ACh b. Noradrenaline
c. Somatostatin d. Motilin

14. HCl is secreted in human by:
a. Parietal cells of stomach
b. Chief cells of stomach
c. B-cells of pancreas
d. I-cells of small intestine

15. Achalasia is a condition that represents a state of:
a. Pyloric stenosis
b. Persistent opening of LOS
c. Failure of LOS opening on arrival of food bolus
d. None of these

16. The enzyme that converts trypsinogen to trypsin in the duodenum is:
a. Enterokinase b. Gelatinase
c. Elastase d. Lipase

17. Rhythmic segmental contractions of small intestine are initiated:
a. Myogenically
b. By neural stimulation
c. Hormonal stimulation
d. None of the above

18. Peristalsis of small intestine has:
a. Neural origin b. Hormonal origin
c. Myogenic origin d. None of these

19. Lipid-soluble bilirubin is converted into water-soluble bilirubin by:
a. Liver b. Kidney
c. Bone marrow d. Small intestine

20. Mass peristalsis is seen in:
a. Liver b. Colon
c. Small intestine d. Stomach

ANSWER KEY

1. b	**2.** a	**3.** a	**4.** b	**5.** b	**6.** c	**7.** d	**8.** c	**9.** a	**10.** b
11. d	**12.** b	**13.** d	**14.** a	**15.** c	**16.** a	**17.** a	**18.** a	**19.** a	**20.** b

Rapid Review Questions and Answers

GASTROINTESTINAL TRACT

1. Name the layers of GIT wall from outside to inside.

Ans.

- Serous layer
- Muscular layer
  - Outer longitudinal
  - Inner circular (form sphincters at different places)
- **Submucosal layer:** Contains blood vessels and lymphatics.
- **Mucosal layer:** Contains glands, muscularis mucosa, lamina propria
  - Thrown into folds called villi.

2. What is the nerve supply to the GIT?

Ans. Intrinsic innervation (Enteric nervous system)

- **Myenteric plexus (Auerbach's plexus):** Present between the longitudinal and circular muscle layer. It has motor function. It controls GIT peristalsis.
- **Meissner's plexus**: Present between the circular muscle and submucosa. It controls:
  - Motility of villi
  - Exocrine and endocrine secretions
  - Local blood flow
  - Detect distension of the gut wall

Extrinsic Innervation

	PSNS	SNS
i.	↑ Motility of GIT	↓ Motility of GIT
ii.	Relaxation of the sphincters	Contraction of sphincters
iii.	↑ GIT secretions	↓ GIT secretions
iv.	↑ Blood flow to GIT	↓ Blood flow
v.	↑ GIT hormone secretion	↓ Villi movements

3. Name the glands present in the small intestine.

Ans.

- Crypts of Lieberkuhn
- Brunner's glands

4. What is the rate of turnover of intestinal epithelium?

Ans. Once in 3-days old cells are replaced by new cells - This is essential for normal GIT function.

5. What are the higher centers that influence GIT function?

Ans. *Cerebral cortex, limbic system* and *hypothalamus influence GIT.*

- Secretions.
- Motility.

6. Name the salivary glands and mention their contribution to total salivary secretion.

Ans.

Parotid gland 20–30 g	Submandibular 8–10 g	Sublingual 2–3 g
Contain only serous cells	Contain serous and mucous cells 4:1 ratio	Contain serous and mucous cells 1:4
Contribute 20–25%	70%	5%
Stensen duct	Wharton's duct	Ducts of rivinus

7. What is the source for Parasympathetic nerve supply?

Ans.

- Superior *salivary nucleus* provides PSNS fibers *to submaxillary and sublingual glands.*
- Inferior *salivary nucleus* provides PSNS fibers *to parotid gland.*

8. What is the effect of nerves on salivary secretion?

Ans.

- **PSNS:** Increases watery saliva high in enzymes.
- **SNS:** Increases secretion of thick viscous saliva containing mucus and enzymes.

9. What is the difference between primary and secondary saliva?

Ans.

- **Primary saliva:** Produced by acinar cells - *Isotonic* to plasma.
- **Secondary saliva:** Absorption of Na^+, Cl^- and secretion of K^+, HCO_3^- by duct cells makes the saliva *hypotonic.*

10. What are the functions of Saliva?

Ans.

- *Digestion* of starch by Amylase to alpha dextrins and maltose. Lipids are digested by lingual lipase.
- **Mucin:** Lubricates the oral cavity, Facilitates swallowing, Bolus formation.

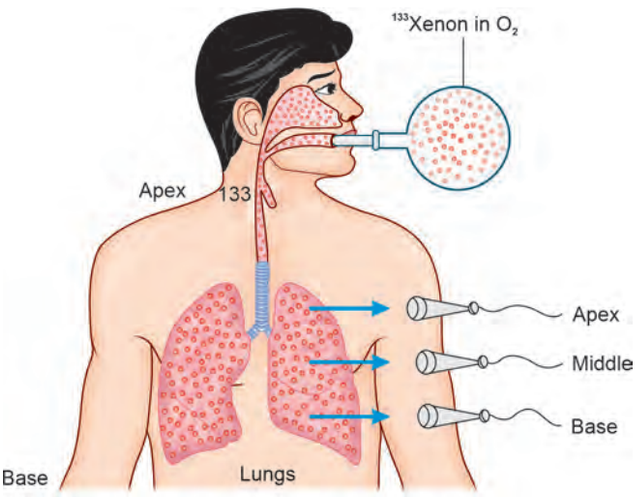

Fig. 95.3: Assessment of uniformity of ventilation by ^{133}Xenon isotope

the apex. It is due to the influence of gravity. Non-uniform ventilation can be detected by certain techniques.

Using ^{133}Xenon Isotopes

The subject is asked to inhale a radioactive isotope of the inert gas Xenon-133. A battery of radiation detectors is placed over the chest and radioactivity is monitored. Areas that show little radioactivity are poorly ventilated. These areas are called *cold spots.* Areas with over ventilation are called *hot spots* (Fig. 95.3).

PERFUSION OF LUNGS

Lungs are perfused with venous blood. About 5 liter of blood flows through both the lungs per minute. In erect posture, lung perfusion gets affected by gravitational influences. The perfusion gradually increases from the apex toward the base. The flow of blood to a given region of the lung is dependent on (i) alveolar pressure (PAlv), (ii) pulmonary arterial pressure (PAP) and (iii) pulmonary venous pressure (PVP). Alveolar pressure in the apical region is more and hence perfusion is low. Alveolar pressure declines toward the base and hence perfusion gradually increases toward the base. *The perfusion pressure of lung capillaries is lower than the colloidal osmotic pressure and hence edema does not develop in the lungs.*

Alveolar perfusion is not uniform even in healthy individuals due to the influence of *gravity.* Base receives more blood flow than the apex.

Detection of Nonuniformity of Lung Perfusion

^{133}Xenon is mixed in saline solution and is injected into superior vena cava through a catheter. As the blood enters the pulmonary capillaries, Xenon is liberated into the alveoli

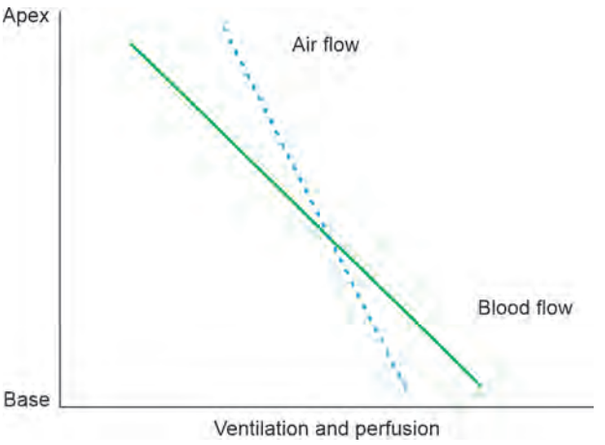

Fig. 95.4: Effect of gravity on ventilation and perfusion of alveoli

because of its low solubility. Radio detectors are placed over the chest and the radioactivity emitted can be noted. If this is uniform, then the perfusion of the lungs must be considered as normal. From this, 1. regional variation in perfusion can be detected, 2. Nonuniformity of lung perfusion can be detected in the form of *cold* and *hot spots.*

Gravity Effects on Blood and Gas Flow to the Lungs

For efficient transfer of gases between the blood and the alveoli, the alveoli should receive an adequate air and blood supply. Air and blood supply to alveoli varies greatly from one part of the lung to another. The main reason for this variation is the effect of gravity. In man, normal posture is standing. This causes a greater air and blood flow to the base than to the apex (Fig. 95.4).

VENTILATION-PERFUSION RATIO (PY6.2)

Pulmonary blood flow/minute is 5 L and alveolar ventilation is 4.2 L/min (12 × 350). *The ratio between ventilation and perfusion of lung is called ventilation-perfusion ratio.*

$$\text{Normal ratio} = \frac{4.2}{5} = 0.84 = \text{V/Q}$$

RECALL What is the physiological significance of panting and snorkeling (breathing by a swimmer using a tube)? What is their effect on dead space and alveolar ventilation?

Each lung normally displays the same ratio. Non-uniformity of ventilation/perfusion ratio may cause abnormalities in the oxygenation of blood.

When a person is in supine, blood flow is nearly uniform throughout the entire lung. When standing, however, the lungs are divided into three zones based on blood flow and ventilation as affected by gravity, with zone 1 at the apices,

- In the testes for maintaining high levels of testosterone and for maintaining temperature at 32°C in the seminiferous tubules.

Factors that influence peritubular osmolality gradient

Number of juxtamedullary nephrons and length of LH: Mainly juxtamedullary nephrons take part in the counter-current mechanism, so the concentrating power of the kidney goes with the number and length of loops of Henle.

Rate of the fluid flow in the tubule: A rapid flow of fluid through the tubule causes decreased absorption of urea by reducing the gradient for the urea absorption. This weakens the urea cycle, and so peritubular osmolality is affected.

Urea availability: Urea has a definite role in producing peritubular osmolality gradient as evidenced by the urea cycle. So, concentrating ability of the kidney increases with the availability of urea.

Blood flow through vasa recta: Vasa recta acting as a counter-current exchanger maintains the osmolality gradient. As increase in blood flow through vasa recta washes away the Na^+, so, Na^+ cycle becomes weaker. This results in a decreased peritubular osmolality gradient. A decreased blood flow through vasa recta increases the peritubular osmolality gradient.

Lymphatic drainage: Disruption of the renal lymphatics decreases renal concentrating ability. When lymphatics are blocked, protein accumulates in the medullary interstitium, which reduces the osmolality gradient.

ADH: *See role of ADH under heading Role of Antidiuretic hormone.*

Importance of Peritubular Osmotic Gradient: Peritubular osmotic gradient is necessary for the absorption of (a) H_2O from the descending limb of LH and (b) H_2O from DCT and CD.

Peritubular osmotic gradient and ADH have complementary role in the production of concentrated urine. Thus, due to absorption of H_2O there is reduction in the volume of urine, and at the same time increase the concentration of urine.

Role of Antidiuretic Hormone

ADH is essential and plays a major role in the production of concentrated urine by the following actions:

- ADH increases H_2O absorption from last part of DCT and CD by increasing the number of *aquaporin* (AQP) channels on the luminal side of the tubular epithelial cell membrane.
- It stimulates the rate of absorption of Na^+, K^+, $2Cl^-$ from the thick ascending limb of LH, thereby potentiating the counter current mechanism, which in turn improves the cortico-medullary osmotic gradient.
- ADH increases the absorption of urea from the inner most medullary collecting duct by facilitated diffusion (urea cycle).
- Vasopressin by its vasoconstrictor effect decreases blood flow through vasa recta.

Net Effect

Medullary peritubular osmotic gradient is generated by:

- Na^+ and Cl^- outflow from the AL of LH.
- Urea cycle between AL and CD.
  - Each one contributes 50% to medullary osmotic gradient.
  - ADH is essential not only for generation of medullary osmotic gradient, but also for production of concentrated urine.

Thus in the absence of ADH, there is a decrease in peritubular osmolality and increase in the production of dilute urine.

Changes in the Tubular Fluid During Formation of Concentrated Urine

Proximal tubule: The fluid in the PCT is iso-osmotic with plasma. About 60–70% of water and other substances are absorbed into the blood. Tubular fluid is iso-osmotic at the end of the PCT.

Descending limb: As the peritubular osmotic gradient from corticomedullary junction to the renal papilla increases from 300–1200 mOsm, lots of water is absorbed from the descending limb of LH. As a result, at the bend, the *osmolality of tubular fluid* becomes equal to medullary interstitial fluid (1200 mOsms).

Ascending limb of LH: Throughout ascending limb of LH, Na^+, Cl^-·, K^+ are absorbed causing a decrease in the osmolality of the tubular fluid (150 mOsms).

Early distal tubule: The tubular fluid in this segment becomes further diluted due to further absorption of Na^+ and Cl^- and attains osmolality of 100 mOsms.

Late DCT and cortical collecting ducts: Water is absorbed from this segment under the influence of ADH. As a result, the osmolality of the tubular fluid increases.

Medullary collecting duct: ADH further increases the concentration of the tubular fluid by increasing H_2O absorption.

Urea concentration gradually increases in the tubular fluid and diffuses out from the inner medullary collecting duct. ADH facilitates the urea absorption from this segment. *The osmolality of the tubular fluid gradually increases from 150 mOsm/L in the diluting segment to 1200 mOsm/L at the end of the inner medullary duct.* Thus concentrated urine as less as 0.5 L/day is produced in the presence of ADH.

Applied Physiology

Kidney fails to produce concentrated or diluted urine in the following conditions:

- **Osmotic diuresis:** Large amounts of isosmotic urine is produced due to the osmotic effects of glucose or electrolytes. This is seen in diabetes mellitus and diuretic therapy.
- **Water diuresis:** Increased formation of dilute urine is seen in (a) Excess drinking of water, (b) ADH deficiency (diabetes insipidus).
- Water diuresis in *nephrogenic diabetes insipidus.*
- Syndrome of inappropriate hypersecretion of ADH *(SIADH).* **SIADH** is associated with formation of concentrated urine due to absorption of H_2O and excretion of Na^+ and other electrolytes.

Rapid Review Questions and Answers

1. **What are the parts of renal system?**
   Ans. i. Two kidneys, ii. Two ureters, iii. Bladder, iv. Urethra.
2. **Explain the non-excretory functions of kidneys.**
   Ans.
   - **Regulation of serum electrolytes:** In excess, they are excreted into urine and in deficiency electrolytes are reabsorbed.
   - **Regulation of blood pH:** By altering H^+ secretion into urine.
   - **Regulation of blood volume:** By conserving or eliminating H_2O, blood volume is regulated.
   - **Regulation of blood pressure:** Renin-angiotensin-aldosterone mechanism participates in this.
   - **Hormone production:** a EP, b Renin, c 1,25 (OH)2 cholecalciferol, d Thrombopoietin.
3. **What is the functional unit of kidney? Give the total number of nephrons.**
   Ans. Nephron is the functional unit of kidney. It measures *45–65* cm is the functional unit of kidney.
   Total no. of Nephrons: *2–3 millions/Two kidneys.*
4. **What is the reserve in kidney function?**
   Ans. It is 75.
5. **Name the parts of a nephron.**
   Ans. Parts of a nephron are:
   - **Renal or malpighian corpuscle**
   - **Proximal convoluted tubule (PCT)**
   - **Loop of Henle (LH)**
   - **Distal convoluted tubule (OCT)**
   - **Collecting duct (CD**
6. **How does PCT differ from Distal nephron (DCT and CD in structure and function?**
   Ans.
   - **PCT** is made up of *epithelia with brush border*. A definite % of absorption *(65–70% filtrate)* irrespective of the need takes place.
   - **Distal nephron** does not *have brush border* epithelia. It is made up of principal and intercalated cells. Absorption from this depends on the *needs of the body.*
7. **Which nephrons are more important?**
   Ans. Cortical nephrons are more important as they participate in the excretion of metabolic waste products.
8. **What is reno-renal reflex?**
   Ans. An increase in *ureteral pressure* in one *kidney* reflex leads to a *decreased SNS action* on the *contralateral kidney*, which *helps* in increasing its excretion of Na^+ and H_2O.
9. **Differentiate cortical from juxtamedullary nephrons.**
   Ans.

Cortical nephrons	Juxtamedullary nephrons
• Number 85%	• 15%
• Present in the renal *cortex*	• Present in the renal *medulla*
• *Short* Loop of Henle	• Long Loop of Henle
• *LH* reaches *outer medulla* only	• LH reaches *inner medulla*
• Surrounded by peritubular capillary *plexus*	• **Vasa recta** accompany the LH
• Fluid flows *faster*	• Fluid flows *slower*
• Participate in *reabsorption of filtered substance* and excretion of waste products	• Participate in *countercurrent mechanism* and in the *formation* of *concentrated urine*

10. **What are the components of Juxtaglomerular apparatus? Mention their functions.**
    Ans. JG apparatus is located at the point of contact of DCT with afferent and efferent arterioles.
    Components
    - **Juxtaglomerular cells**
      - Modified vascular smooth muscles (afferent arteriole).
      - Synthesize store and release renin.
      - Act as baroreceptors.
      - Respond to hypovolemia and ↓, BP.
    - **Macula densa cells**
      - Modified renal epithelial *cells of DCT.*
      - Function as chemoreceptors.
      - Detect Na^+, Cl^- concentration in the luminal fluid.
      - Influence renin release *from JG cells.*

APPENDIX I

Clinical Case Scenario and Solution

1. A middle-aged man with a bullet wound on the 8th thoracic vertebra on the right side reported to the OPD. He was found to have the following clinical findings.
- A strip of anesthesia on the same dermatomal distribution on the same side.
- Loss of vibratory and proprioceptive sensations below the lesion on the same side and loss of the pain and temperature on the opposite side.
- Babinski response was positive on the injured side.

a. What is your diagnosis?
b. How do your explain loss of pain and temperature on the opposite side?
c. Name the tracts that carry vibration and proprioception.

2. A 50 year old man with a stooped posture consulting a neurologist was found to have a resting coarse tremor, which disappeared on voluntary movement, expressionless face and a short shuffling gait. He showed muscular rigidity.
a. What is the diagnosis?
b. What is the treatment advocated?
c. What is the cause for this disease?

3. A 55-year-old lady complained of having polydipsia and polyuria and increased thirst,
a. Give probable causes for the above symptoms.
b. What diagnostic tests do you advocate to arrive at diagnosis?
c. What is the cause for the above features when the hormone levels are normal

4. A young boy of 14 years reported to OPD with the history of fever and oliguria, swollen legs (edema) and breathlessness. On investigation, he had proteinuria and pitting edema.
a. What is the diagnosis?
b. Give the reason for edema.
c. Mention normal plasma proteins levels.

5. A middle-aged person was brought to casualty in an unconscious state. On examination, his BP was low and pulse rate was high. Electrocardiogram showed myocardial infarction.
a. What is your diagnosis?
b. What is the cause for the unconscious state?
c. What is the cause for high heart rate?

6. A motorcycle rider met with an accident and was brought to the causality in an unconscious state. He had several injuries resulting in loss of blood. On examination, his BP was very low and showed a low volume rapid pulse rate with cold, pale and clammy skin.
a. What is the probable diagnosis?
b. Suggest the line of treatment for this patient.
c. How will you explain the signs and symptoms?
d. How will you manage when the blood loss is 25%?

7. An old lady sitting on the terrace of the house fell down on the ground, her head hitting the wall. She was brought to the casualty in an unconscious state. On examination, she had very low BP with rapid pulse rate. There was no loss of blood due to injury.
a. What is the probable diagnosis?
b. How do you explain the unconscious state?
c. What is syncope? Explain with one example.

8. A young boy fell down and injured his spinal cord. He was examined by the neurologist and found normal tendon reflexes in the upper limbs. His abdominal reflexes were normal after few weeks. He showed Babinski Positive with exaggerated knee jerk and ankle jerk.
a. What is the probable site of spinal injury?
b. What is the cause for Babinski positive sign?
c. What is ankle clonus?
d. What is spinal shock? Give the cause.

9. A person of above 50 years reported to OPD complaining of some neurological problems. On examination, he was unable to speak properly. He was unable to move his finger along the line and stop at the right point. He showed drunken gait and could not do supination and pronation of upper limb at a rapid rate.
a. What is the probable diagnosis?
b. Name two tests for the confirmation of diagnosis.
c. Differentiate sensory ataxia from motor ataxia.

APPENDIX II

Numerical Formulas for Quick Review

1. **Nernst equation** = $E_{ion} = \frac{RT}{ZF} \text{In} \frac{C_{in}}{C_{out}} = 61.5 \log \frac{C_{in}}{C_{out}}$

   Here, E = Equilibrium potential

2. **Goldman – Hodgkin – Katz constant field equation**

   $$V = \frac{RT}{F} \text{In} \frac{Pk(K_o^+) + PNa(Na_o^+) + PCl^-(Cl_{in}^-)}{Pk(K_i^+) + PNa(Na_i^+) + PCl^-(Cl_{out}^-)}$$

   Here, V = Voltage across the membrane (RMP)

3. **Total body water (TBW) (V)**

   $$= \frac{\text{Amount of substance (A) injected}}{\text{Average concentration of the Substance/m/(c)}}$$

4. **Extra cellular fluid volume (ECFV) (V)**

   $$= \frac{\text{Amount of substance injected (A)} - \text{Amount excreted (x)}}{\text{Average concentration of the Substance/m/(c)}}$$

5. **Determination of plasma volume**

   $$\text{Plasma volume} = \frac{100 - PVC}{100} \times \text{Blood volume}$$

6. **Determination of blood volume**

   $$\text{Blood volume} = \frac{\text{Plasma volume}}{100 - PCV} \times 100$$

7. **Conduction velocity of nerve impulse**

   $$= \frac{\text{Length of nerve in millimeter}}{\text{Conduction time in milliseconds}}$$

8. **Work done** = Force (weight) × Distance lifted

9. **Mechanical efficiency** = $\frac{\text{Work done}}{\text{Energy consumed}} \times 100$

10. **Color Index** = $\frac{\text{Percentage of Hb}}{\text{Percentage of RBC count}}$

    15 mg = 100%

    5 million/μm = 100%

    Normal = 0.9 – 1.1

11. **Mean corpuscular Volume (MCV)**

    $$MCV = \frac{\text{Volume of PCV in m/100 mL}}{\text{RBC in million/μL}} \times 10$$

    Normal range = 78 – 94 μ^3

12. **Mean corpuscular hemoglobin (MCH)**

    $$MCH = \frac{\text{Hb in gms/100 mL}}{\text{RBC in millions/μL}} \times 10$$

    Normal = 28 – 32 Pg

13. **Mean corpuscular hemoglobin concentration (MCHC)**

    $$MCHC = \frac{\text{Hb in gms/100 mL}}{\text{PVC/100 mL}} \times 100 \quad \text{or} \quad = \frac{MCH}{MCV} \times 100$$

    Normal = 32 – 38%

14. **Duration of cardiac cycle** = $\frac{\text{One minute}}{\text{Heart rate}}$

15. **Heart rate** = $\frac{\text{One minute}}{\text{Duration of cardiac cycle}}$

    From ECG = $\frac{1500 \text{ mm}}{\text{R R interval in mm}}$

16. **Einthoven's law** = LI + LIII = LII or LI + LIII – LII = 0

17. **Ejection fraction (EF)** = $\frac{\text{Systolic volume}}{\text{End diastotic volume}} \times 100$

    Normal = 55 – 65%

18. **Cardiac output (CO)** = Stroke volume × Heart rate

19. **Stroke volume (SV)** = End diastolic volume – End systolic volume

    = 70 – 80 mL

20. **End systolic volume (ESV)**

    = End diastolic volume – Stroke volume

    = 130 – 70 = 60 mL/ventricle

21. **Cardiac Index (CI)** = $\frac{\text{Cardiac output (CO)}}{\text{Body surface area (SA)}}$

    Normal = 2.5 – 3.1 L/m^2/min

22. **Fick principle**

    Amount of substance taken by organ (X)

    = A – V difference of that substance × Blood flow (Q)

    Blood flow (Q)

    $$= \frac{X}{\text{A – V difference of a given substance per 100 mL}} = \text{mL/min}$$

23. **Cardiac reserve**

    = CO during exercise – Resting CO

    = 25 – 5 = 20 L/min = $\frac{20}{5} \times 100 = 400\%$

APPENDIX III

Physiological Problems and Solutions

1. Calculate the bold volume with the following data:
   - Amount of dye injected = 5 mg
   - Average concentration of the dye in the plasma = 1.6 mg/L
   - Hematocrit value = 45%
2. Calculate alveolar ventilation using the following data:
   - Tidal volume = 500 mL
   - Dead space = 150 mL
   - Respiratory rate = 12/min
3. Find out breathing reserve (BR) and dyspnoeic index (DI) using the following data:
   - Maximum voluntary ventilation (MVV) = 100 L/min
   - Pulmonary ventilation (minute volume) (PV) = 8 L/min
4. Calculate blood indices with the following data:
   - Hb content = 15 g%
   - RBC count = 5 min/mm^3
   - PCV = 45%
5. Calculate RQ of a person taking a mixed diet with the following data:
   - O_2 consumption per minute = 250 mL/min
   - CO_2 output per minute = 200 mL/min
6. Calculate renal blood flow from the following data:
   - Urinary PAH (UPAH) = 14 mg/mL
   - Plasma PAH (PPAH) = 0.02 mg/mL
   - Volume of urine = 0.9 mL/min
   - PAH extraction ratio = 0.9
   - Hematocrit = 45%
7. Calculate the GFR with the following data:
   - Urine inulin = 35 mg/mL
   - Volume of urine = 0.9 mL/min
   - Plasma inulin = 0.25 mg/mL
8. Calculate filtration fraction from the following data:
   - GFR = 125 mL/min
   - Renal plasma flow = 625 mL/min
9. Calculate cardiac output with the following data:
   - O_2 consumption = 250 mL/min
   - Arterial O_2 concentration = 190 mL/min
   - Venous O_2 concentration = 140 mL/L
10. Calculate cardiac output and stroke volume from the following data:
    - Heart rate = 80/min
    - Total amount of indicator injected = 5 mg
    - Average concentration of the indicator in 40 seconds = 1.6 mg/L
11. Calculate O_2 carrying capacity and O_2 content of arterial blood.

    When Hb concentration is 14g % and arterial saturation is 80%.
12. Calculate extracellular fluid volume from the following data:
    - Amount of sucrose administered = 150 mg
    - Amount of sucrose excreted = 10 mg
    - Concentration of sucrose in plasma = 0.01 mg/mL
13. Calculate the dead space from the following data:
    - PCO_2 of alveolar air = 40 mm Hg
    - PCO_2 of expired air = 28 mm Hg
    - Tidal volume = 500 mL
14. Calculate effective filtration pressure in the glomerular capillaries from the following data:
    - Hydrostatic pressure in glomerular capillaries = 60 mm Hg
    - Hydrostatic pressure in Bowman's capsule = 15 mm Hg
    - Volloidal osmotic pressure of blood in the glomerular capillaries = 28 mm Hg
15. Calculate free water clearance with the given data:
    - Plasma osmolarity = 300 m.Osm/L
    - Urine osmolarity = 600 m.Osm/L
    - Urine flow rate = 1 mL/min
16. Calculate the urea clearance from the following data:
    - Concentration of urea in urine (U) = 15 mg/mL
    - Concentration of urea in blood (B) = 40 mg/100 mL
    - Rate of urine flow (V) = 2 mL/min
17. Calculate the heart rate of a person, when his R-R interval in 20 mm and the speed of the paper is 1500 mm/min.
18. Calculate the cardiac index of an individual from the following data:
    - O_2 consumed = 250 mL/min
    - A – V difference in O_2 = 5 mL/100 mL
    - Body surface area = 1.7 m^2

LPR Fundamentals of Medical Physiology

Salient Features

- This 8th edition of LPR's Fundamentals of Medical Physiology is duly updated with all the latest concepts of physiology.
- It is based on the requirements of Competency-Based Medical Education (CBME) curriculum which are mentioned and marked along with the topics.
- Each and every chapter has been designed in a manner to facilitate better learning and easy retention of the concepts.
- Each chapter starts with competency numbers which are categorized as must know topics for the students.
- Clinical correlation of a topic connects to clinical situation, and its physiological bases are added.
- Recent concepts are simplified, added and are made student friendly for quick learning.
- Applied physiology topics and clinical case scenarios are added as per the requirement of the latest curriculum.
- 1500+ colorful hand-drawn figures and images relevant to the topics are added liberally to make the content more student friendly.
- Complex and difficult topics have been supplemented with numerous tables and flowcharts for easy and quick understanding.
- Self-assessment review exercises with a variety of questions, like Short Notes, Clinical Questions, Multiple Choice Questions have been added for assessing the preparation after completing the respective section.
- Thought-provoking questions along with flowing matter help the student for instant recollection of the relevant points as Recall Box.
- Newly-added content in the book as per the CBME-2019:

  (See Under Section I: General Physiology)
  - **Chapter 1:** Introduction to Physiology [Containing Scientists' Contributions to Physiology](Vol. 1)

  (See Under Section XIV: Integrated Physiology)
  - **Chapter 12:** Cytological Methods and their Applications in Clinical Care and Research (Vol. 2)
  - **Chapter 13:** COVID-19 (Vol. 2)
  - **Chapter 14:** Acquired Human Immunodeficiency Syndrome (Vol. 2)
  - **Appendix I:** Clinical Case Scenario and Solution
  - **Appendix II:** Numerical Formulas for Quick Review
  - **Appendix III:** Physiological Problems and Solutions
- Newly-added topics, like Criterion for Brain Death Confirmation, Gut-Brain Axis, Gut-Brain-Heart Axis, Pregnancy-Psychological-Psychiatric Disorders, Psychological and Psychosocial Changes Associated with Puberty and many more enrich the content.

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