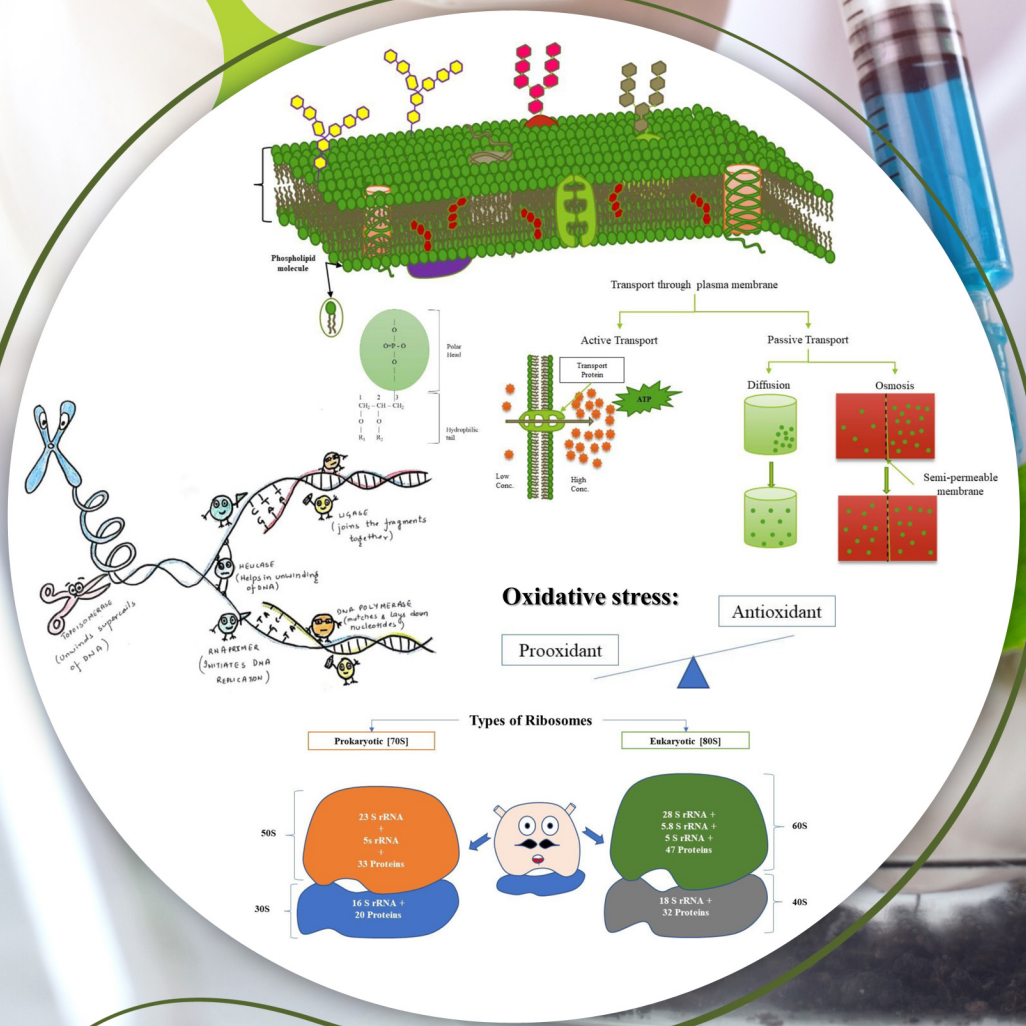
MIND MAPS IN BIOCHEMISTRY



Simmi Kharb

Bentham Books

Mind Maps in Biochemistry

Authored by

Simmi Kharb

Department of Biochemistry, and Nodal Officer, Multidisciplinary Research Unit,
Pt. B. D. Sharma Postgraduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana 124001, India

Mind Maps in Biochemistry

Editor: Simmi Kharb

ISBN (Online): 978-981-14-7790-4

ISBN (Print): 978-981-14-7788-1

ISBN (Paperback): 978-981-14-7789-8

need for a court order if at any point you breach any terms of this License Agreement. In no event will any delay or failure by Bentham Science Publishers in enforcing your compliance with this License Agreement constitute a waiver of any of its rights.

3. You acknowledge that you have read this License Agreement, and agree to be bound by its terms and conditions. To the extent that any other terms and conditions presented on any website of Bentham Science Publishers conflict with, or are inconsistent with, the terms and conditions set out in this License Agreement, you acknowledge that the terms and conditions set out in this License Agreement shall prevail.

Bentham Science Publishers Pte. Ltd.
80 Robinson Road #02-00
Singapore 068898
Singapore
Email: subscriptions@benthamscience.net

CONTENTS

FORWORD i

PREFACE iii

CHAPTER 1 CELL, PLASMA MEMBRANE, MEMBRANE TRANSPORT 1

CHAPTER 2 INTRODUCTION OF METABOLISM: ANABOLISM, CATABOLISM AND ENERGY METABOLISM 32

CHAPTER 3 CHEMISTRY OF CARBOHYDRATES 55

CHAPTER 4 METABOLISM OF CARBOHYDRATES 64

CHAPTER 5 CHEMISTRY OF LIPIDS 87

CHAPTER 6 METABOLISM OF LIPIDS..... 94

CHAPTER 7 CHEMISTRY OF PROTEINS 120

CHAPTER 8 METABOLISM OF PROTEINS 126

CHAPTER 9 INTERMEDIARY METABOLISM..... 148

CHAPTER 10 CHEMISTRY OF NUCLEOTIDE..... 153

CHAPTER 11 NUCLEOTIDE METABOLISM..... 157

CHAPTER 12 MOLECULAR BIOLOGY 169

CHAPTER 13 GENETIC ENGINEERING 215

CHAPTER 14 MAINTENANCE OF BODY COMPOSITION..... 222

CHAPTER 15 CLINICAL BIOCHEMISTRY, PHYSIOLOGY & GENETIC DISORDERS 285

CHAPTER 16 THE ENDOCRINE SYSTEM 337

SUBJECT INDEX 355

FOREWORD

Undersigned is excited to record personal impressions on book, "Mindmaps in Biochemistry" authored by Dr. Simmi Kharb working at Department of Biochemistry, Pt**.** B. D. Sharma Postgraduate Institute of Medical Sciences **(**PGIMS**)**, Rohtak, Haryana, India as a Professor and Nodal Officer at the Multidisciplinary Research Unit of the Institute.

The first textbook on Biochemistry was written by Alexander Thomas Cameron in 1928. Since then, ginormous development has taken place in the field of Biochemistry into different scientific canals. On one hand the whole genome has been unfurled and on other hand, there has been great demand of traditional knowledge. When the world is passing through turmoil of knowledge bank, there has been great development in understanding the 'Chemistry of Biological Systems'. Professor Simmi Kharb has generated literature by virtue of her book in the arena of Biochemistry with an aim (ambition in mind) that the present day students studying Biochemistry need comprehensive information at one place in understandable language that can act as unstoppable orientation in young minds that would lead to formation of strong grass root for becoming passionate Biochemists.

It was being felt by the teachers and students of Biochemistry that a composite collection of Biochemical Principles which can find place in the minds of learners just like map, was missing in the literate world. Dr. Simmi Kharb accepted the challenge of producing a book on Biochemistry that has simple, consolidated, easy to read and retain, all in one, mixture of basic and advanced knowledge module.

The issues covered in this book are: Biochemical concepts, Organization of chemical and biological approach, Principles in balance of biological systems, Acquiring meaningful understanding of Biochemistry, Real-time world relevance and Problem-solving mechanisms. The book runs through cell to body.

I am confident that this book shall make its place in libraries, minds of teachers and vocal cord of students all over the world.

Gajendra Singh, Ph.D
Professor and Dean
Faculty of Pharmaceutical Sciences
Pt. BD Sharma University of Health Sciences
Rohtak 124001
Haryana
India

PREFACE

Students often view Biochemistry as a pile of facts or equations to be memorized rather than as concepts to be understood. The author proposes to create a series of concept and knowledge maps about the biochemical contents to illustrate graphically the relationships between the ideas presented in a given proposed chapter, as well as to show how information can be grouped or organized.

In order to facilitate the student's understanding of the metabolic pathways and providing greater interaction with the contents, an approach to better learning metabolic diagrams will be developed through:

i. Flow diagrams and illustrations: showing substrates and enzymes of the metabolic pathways, their control, inhibition, role of vitamins in their correct functioning, and their connection with other systems
ii. Reading the functions and characteristics of metabolic pathways in illustrations
iii. Solving of essay and multiple-choice questions
iv. Recent advances and applied aspects of biochemistry, applied therapeutics and microbiology will be discussed

Also, students will be encouraged to make their own flow diagrams and tables and sample questions will be provided to improve their analytical skills.
As a learning tool, it can be used by the student to, *e.g*., making notes, solving problems, planning the study and/or writing of essays, preparing for examinations, and identifying the connection of topics.

ACKNOWLEDGMENT & CONFLICT OF INTEREST

No potential conflict of interest is declared by the author. It is also declared the complete work is an individual effort by the author and there was no financial/ administrative/ academic support availed from any individual/ institution /organization.

Simmi Kharb
Department of Biochemistry
Nodal Officer, Multidisciplinary Research Unit
Pt. B. D. Sharma Postgraduate Institute of Medical Sciences (PGIMS)
Rohtak, Haryana 124001
India

CHAPTER 1

Cell, Plasma Membrane, Membrane Transport

LEARNING OBJECTIVES: • Illustrate the cellular components and their significance. • Appraise the structure and function of the cell membrane. • Explain the transport mechanisms operating across the plasma membrane.	**Keywords:** Active transport, Eukaryotic cells, Prokaryotic cell, Plasma membrane, Passive transport, Sub-cellular component.

KEY FEATURES OF CELL	Cells possess a genetic program and the mean to use it: capable of producing more of themselves. Cells acquire and utilize energy, carry out a variety of chemical reactions: metabolism. Cells engage in mechanical activity able to respond to stimulant. **PROKARYOTIC CELL** Lack well-defined nucleus. Contain rigid cell wall. **EUKARYOTIC CELL** Cells are highly complex and organized. Contain well defined nucleus, more complicated internal structure.

1. Cell: structural and functional unit of life.
2. Most chemical reactions take place within cells.
3. Cells are of two types:
    i. Prokaryotic cell
    ii. Eukaryotic cell

- The human body is composed of 10^{14} cells.

Comparison	**Prokaryotic Cell**	**Eukaryotic**
Size	Small 1-10μ	Large 10-100μ

Simmi Kharb

Cell Wall	Present	As extracellular matrix
Cell Membrane	Rigid, cell wall	Flexible, plasma membrane
Nucleus	No well-defined nucleus	Well-defined nucleus, contain membrane
DNA	Found as nucleoid	DNA associated with histones
Histones	Absent	Present
Nucleolus	Absent	Present
Genome	Single, circular chromosome	Multiple chromosomes
Metabolism	Both aerobic and anaerobic	Aerobic
Respiratory Enzymes	Located in the plasma membrane	Located in mitochondria
Cell Division	Cleavage, fission	Mitosis, meiosis
Cytoplasm	Lack organelle and cytoskeleton	Contain organelle and cytoskeleton

CYTOSOL

Fluid compartment: soluble part, viscous gel.

Represents 50-60% of total cell volume

It is in contact with all sub-cellular organelle.

Contains: enzyme, metabolites and salts.

Functions

Carbohydrate metabolism

Fat metabolism

Nucleotide metabolism

COMPOSITION OF CYTOSOL

1. **Proteins:**
   - ***a. Enzymes***
     - i.Carbohydrate metabolism
     - ii.Protein metabolism
     - iii.Fat metabolism
   - ***b. Transporter, carrier proteins***
2. **Metabolites:**
   Of carbohydrate and amino acid metabolism.
3. **Other Molecules:**
   Na^+, K^+, Ca^{2+}, Mg^{2+}, HCO_3^-, Cl^-, PO_4^-

METABOLIC PATHWAYS IN CYTOSOL

1. Carbohydrate Metabolism

a.Glycolysis

b. PPP

c. Glycogen

2. Fatty Acid Synthesis (*de novo*)

3. Amino Acid Metabolism

a. Oxidation

b. Deamination

c. Decarboxylation

d. Transamination

4. Pathway present:

a. Initial step of:

i. Heme synthesis

ii.Urea synthesis

b. ***Nucleotide synthesis:*** many steps occur in cytosol:

i. CPS II

ii.ATCase

CYTOSKELETON

Composed of:

- ***Actin filament:*** 7 nm thick, attached to adherens junction, reacts with myosin filament during contraction.
- ***Intermediate filament:*** 10 nm thick, attaches to desmosomes and hemidesmosomes.
- ***Microtubules*****:** 25 nm thick, hollow, composed *of α and β tubulin* subunits.

Functions

- Allows cells to move and adopt different shapes.
- Play role in cell division: microtubules form mitotic spindle.
- Cell movement, determining cell shape, axonal transport.

Cilia

Move fluid over epithelial surfaces *e.g.* respiratory tract

Applied aspect

Immotile cilia can cause Kartagener's syndrome:

Sinusitis, Bronchitis, Situs inverses

Immotile cilia caused by:

Fault in motor protein *dynein:* responsible for the rhythmic movement of cilia and flagella.

CELL JUNCTIONS

Four classes of junction that form epithelial cells:

tight, adherens, desmosomes, gap junctions

NUCLEUS

Large fragmental structure bounded by a double membrane, contains nucleolus.

Generally, cells in human body have a single nucleus except**:**

Skeletal muscle cells have many nuclei.

Mature RBC have no nucleus.

CHAPTER 2

Introduction of Metabolism: Anabolism, Catabolism and Energy Metabolism

LEARNING OBJECTIVES:	**Keywords:**
Explain the metabolic role of catabolic and anabolic activities in a cell. Describe the processes of how cell obtain energy to perform 'Cellular work.	ATP, NAD (P)H, Anabolism, Catabolism, Metabolic integration, Sugar phosphates.

QUICK SUMMARY	**MACROMOLECULAR SYNTHESIS**
Metabolism: Five Functional Blocks ***Catabolic Activities*** Foods oxidized to carbon dioxide and water; ATP and NADPH produced. ***Anabolic Activities*** Metabolic intermediates from catabolism converted to a variety of molecules; ATP and NADPH consumed.	***Anabolic Products used to Synthesize Biopolymers****:* ATP principle source of energy. GTP: Protein synthesis. CTP: Phospholipid synthesis. UTP: Polysaccharide synthesis. Photochemical activities. Light energy used to produce ATP and NADPH. Carbon dioxide fixation. ATP and NADPH used to fix carbon dioxide and convert to an intermediate.

Ten Key Intermediates	
Carbohydrates	CoA derivatives
Triose-P, tetrose-P, pentose-P, hexose-P.	Acetyl-CoA, succinyl-CoA

Simmi Kharb

α Keto acids. Pyruvate, oxaloacetate, α -ketoglutarate.	PEP. ADP/ATP and NAD/NADPH couple catabolism to anabolism.

METABOLISM FACT FILE

Intermediates: A number of intermediates that serve crucial roles in intermediary metabolism such as sugar phosphates, pyruvate, oxaloacetate, α -ketoglutarate, acetyl-CoA, succinyl- CoA and PEP.

1. Sugar phosphates: Found in glycolysis, gluconeogenesis, and the pentose phosphate pathway.

a. Pyruvate: Derived from glycolysis and amino acids. Port of entry into the citric acid cycle for glucose-derived carbons.	***b. Oxaloacetate and α -ketoglutarate:*** Citric acid cycle intermediates. Both can be produced from amino acids by deamination.
2. Acetyl-CoA: Consumed in citric acid cycle The common denominator between fatty acids, sugars, and amino acid	***3. Succinyl-CoA:*** A citric cycle intermediate. Place of entry of propionate from dietary sources and odd-chain fatty acid catabolism. Product of amino acid catabolism. Used in heme biosynthesis.

***4. ATP and NADPH*:** Serve critical roles in coupling catabolism and anabolism.

Catabolism: Largely oxidative in nature. Leads to a reduction of cofactors NAD^+ and FAD. ***Catabolic pathways:*** Exergonic and lead to the synthesis of ATP. ATP is then consumed in anabolic, energy requiring pathways. ***Under physiological conditions:*** ➢ Complete oxidation of glucose: • Gives high yields of ATP. ➢ The process is always far from equilibrium	***Anabolic Pathways*:** Reductive with NADPH. Usually serving as an immediate source of electrons. ***NADPH:*** • This coenzyme is reduced in the pentose phosphate pathway. • Additionally, cycles exist to move electrons from NADH to $NADP^+$

ATP Equivalents

The metabolic unit of energy exchange is ATP.

Defined as the amount of energy released upon hydrolysis of ATP to ADP.

ATP Equivalent of Key Metabolic Reactions

ATP hydrolysis: 1.0.

PPi hydrolysis: 1.0.

ATP to AMP and 2 Pi, 2.0.

NADH Oxidation

3.0 ATP (2.5 in mitochondria)

FADH2 oxidation, 2.0 ATP (1.5 in mitochondria).

METABOLIC INTEGRATION

Key Features:

The major organs specialize in the metabolism of particular fuels:

- There is the interplay among liver, muscles, heart, adipose tissue, and brain.
- This ensures that energy demands are met.

For example, glucose:

Can be supplied to other tissues by:

- Liver by gluconeogenesis, glycogenolysis.
- Muscle can produce lactic acid during times of intense energy demands and this lactic acid is sent to the liver for reprocessing into glucose.

Energy demands are ultimately met by diet and humans have a complex system of hormonal regulation to regulate energy storage and appetite.

Brain, stomach, small intestines, pancreas, and adipose tissue play a role in stimulating or suppressing appetite.

CHAPTER 3

Chemistry of Carbohydrates

LEARNING OBJECTIVES	**Keywords:**
• Describe the role of carbohydrates in biochemistry Categorize different types of sugars. • Illustrate structural formulas of different carbohydrates. • Identify and describe isomerism in carbohydrates	Aldoses, Asymmetric carbon, Disaccharide, Enantiomers, Epimers, Glycosaminoglycans, Heteropolysaccharides, Isomerism, Ketoses, Monosaccharide, Oligosaccharide, Polysaccharide, Reducing sugars

CARBOHYDRATES: STRUCTURE AND FUNCTION

Compounds having hydroxyl groups with aldehyde or keto group $(CH_2O)_n$ **Importance** Major fuel for all tissues Structural component of membrane Form carbohydrate with a specific function: Ribose (nucleotides), Galactose (lactose in milk), Glycolipid, Glycoprotein	**Classification** ***Based on no. of Sugar Units*** Monosaccharide, Disaccharide, Oligosaccharide, Polysaccharide ***Based on Functional groups:*** Aldehyde (aldose), Ketone (Ketose)

Class	**Sub-class**	**Examples**	
		Aldose	**Ketose**
Monosaccharide	Triose	Glycerol	Dihydroxy acetone

<table>
<tr><td></td><td>Tetrose

Pentose

Hexose</td><td>Erythrose

Ribose

Glucose</td><td>Erythrulose

Ribulose

Fructose</td></tr>
<tr><td>Disaccharide (Composed of Two Monosaccharides)</td><td>Maltose

Sucrose

Lactose</td><td>2 glucose units α1→ 4 glycosidic bond

α D glucose +β D fructose α1→ β 2 bond

αD galactose + βD glucose1→ β 4 bond</td><td>Disaccharide (Composed of Two Monosaccharides)</td></tr>
<tr><td>Oligosaccharide (Composed of 2-10 Monosaccharide Units)</td><td>Malto-triose</td><td colspan="2">Maltose and α1→6 glucose</td></tr>
<tr><td>Polysaccharide (10 or more monosaccharide unit)</td><td rowspan="4">-</td><td colspan="2">Amylose

αD: α1→4 bond

Amylopectin 24-30, monomers

(αD glucose) 1→4 linkage plus α1→6 branching</td></tr>
<tr><td>Homopolysaccharides</td><td colspan="2">Starch: α1→4 linkage and α1→6 branching and

Glycogen: 12-14 monomers of D-glucose α1→4 linkage and α1→6 branching</td></tr>
<tr><td></td><td>Cellulose</td><td>βD glucose: β1→ 4 bond</td></tr>
<tr><td></td><td>Inulin</td><td>βD fructose</td></tr>
<tr><td></td><td>Dextran (break down product of starch)</td><td>αD glucose linked at α1→6 bond, with few branches</td></tr>
</table>

ISOMERISM		
Asymmetric Carbon	Carbon atom bonded to four different atoms or groups of atoms is asymmetric carbon.	
Isomers	Presence of asymmetric carbon allows the formation of isomers. Number of isomers of a compound depends on the number of asymmetric carbon atoms (n) = 2^n *E.g*. glucose has 4 asymmetric carbon atoms, thus 2^4 = 16 isomers.	
Isomerism	***Reasoning***	***Example***
DL isomerism (stereo isomer)	The same chemical formula differs in the position of –OH group on one or more asymmetric carbon (*E.g*. C5 in glucose). Mirror images of each other.	D, L glucose
Optical isomerism (Enantiomer)	Presence of asymmetric carbon rotate plane polarized light either to right [dextrorotatory, (+)] or to left [levorotatory (-)]	Enantiomer (+) isomer (-) isomer
Epimerism	Differ in the configuration of –OH and –H glucose on C-2, 3 and 4 of glucose, galactose at C_4 and mannose at C-2 Or Conformation that differs only at one carbon atom	Mannose at C-2 Galactose at C-4
Anomerism	Differ in configuration at carbonyl or anomeric carbon α:- OH on anomeric is below the plane of the ring β:- OH is above the plane of the ring	α anomer β anomer
Aldose-ketose isomerism	Same molecular formula differ in the position of carbonyl carbon: Glucose C-1 is aldehyde; fructose C-2 is levo	Glucose and fructose

CHAPTER 4

Metabolism of Carbohydrates

LEARNING OBJECTIVES:	**Keywords:**
• Explain different anabolic and catabolic pathways of carbohydrate metabolism. • Describe the role of different enzymes and hormones involved in carbohydrate metabolism. • Identify the metabolic diseases related to carbohydrates.	Diabetes, Digestion and assimilation of carbohydrates, Enzymes of carbohydrate metabolism, glycolysis, Glycogen metabolism, Gluconeogenesis, Glucose homeostasis, Regulation of glucose metabolism, Tricarboxylic acid cycle.

CARBOHYDRATE STORAGE	**Starch**	**Glycogen**
Storage form of carbohydrates:	Stored in plants Both amylose and amylopectin	Stored in animals Liver and muscle cells

DIGESTION AND ASSIMILATION OF CARBOHYDRATES: Pathway for digestion of carbohydrates:

Substrate		**Site**	**Enzyme**	**Products**
Starch Lactose Sucrose	Fructose Glucose	Mouth ↓	Salivary amylase α1-4 glycosides	Maltose Maltotriose Limit dextrin
		Stomach ↓	NO DIGESTION	
Starch		Intestine	PANCREATIC AMYLASE (α1-4)	Maltose

Polysaccharides	↓		Maltotriose Limit dextrin
	Epithelial brush border	**OLIGOSACCHARIDASE & DISACCHARIDASES**	
Sucrose Maltotriose Maltose α - limit dextrins	↓	Sucrase (α1-4) – Isomaltase (α1-4)	Glucose Fructose
Maltotriose Maltose		Maltase (α1-4) – Glucoamylase (α1-4)	Glucose
Lactose		Lactase (β1-4)	Glucose Galactose
	Portal vein ↓		
	Liver (metabolism) ↓		
	Circulation (glucose) ↓		
	Liver Muscle Adipose tissue		

DEFECTS IN CARBOHYDRATE ABSORPTION

S. No.	**Disease**	**Defect**	**Clinical Feature**
1.	Lactase deficiency	Lactose intolerance	Abdominal discomfort
		Inherited lactase deficiency	Cramps, diarrhea

		Secondary lactase deficiency	Intolerance to milk
2.	Inherited Sucrase deficiency	Sucrase deficiency	Same as lactase deficiency
3.	Disaccharidases deficiency	Disaccharidiuria	Fructose, sorbitol malabsorption
4.	Defect in SGLT-1	Monosaccharide malabsorption	Fructose, sorbitol malabsorption, watery diarrhea

Oral Hydration Therapy:	In cholera infection: NaCl absorption is inhibited, but not the facilitative transport of Na & glucose		
ORS (oral rehydration solution) provides: →		110mM	Glucose
SGLT-1 is not inhibited and in the presence of glucose Na uptake takes place to replenish stores.		99 mM	Na^+
		74 mM	Cl^-
		39 mM	HCO^-_3
		4 mM	K^+

Enzyme	**Site of Production/ Action**	**Substrate**	**Product**
Salivary Amylase	Salivary glands/ Oral cavity	Starch	Disaccharides (maltose), oligosaccharides
Oligosaccharidases	Lining of the intestine; brush border membrane/ Small intestine	Oligosaccharides Disaccharides	Monosaccharides (*e.g.*, glucose, fructose, galactose)
Pancreatic Amylase	Pancreas/ Small intestine	Starch	Disaccharides (maltose), monosaccharides (*e.g.*, glucose, fructose, galactose)

CHAPTER 5

Chemistry of Lipids

LEARNING OBJECTIVES	**Keywords**
• Identify the structure and name the lipids. • Classify the types of lipids. • Understand the biological role of lipids.	Ceramides, Eicosanoids, Fatty acids, Glycosphingolipids, Phospholipids, Saturated and unsaturated fats, Sphingolipids, Sphingomyelin, Triacylglycerols.

Lipids

- Hydrophobic, Insoluble in water-soluble in polar solvents.
- Composed of saturated or unsaturated long-chain hydrocarbons with a carboxyl group at end of chains.
- Important dietary constituent.
- Serve as a source of energy, thermal insulator, an important component of cell membrane, lipoprotein serves transport function, storage for TAG, stored in adipose tissue, precursor for steroid hormones.

Fatty Acids (FA)

Exist as free or esterified to glycerol

General Formula

Saturated fatty acid:

$CH_3 – [CH_2]_n – COOH$

n = number of methylene groups

Nomenclature

Systemic name: number of carbons

Saturated FA are named by chain length

Unsaturated FA are named by position of double bonds

Suffix - *anoic,* followed by acid

- *anoic* for saturated FA

- *enoic* for unsaturated FA

Simmi Kharb

<table>
<tr><td colspan="2">Position of Double Bond

Δ^9: Double bond between C9 and 10 from the carboxylic end.

ω^6: Double bond on sixth carbon from the omega end.</td><td>E.g. Palmitic acid, 16C: hexadecanoic acid.</td></tr>
<tr><td colspan="2">Naming
Carbons are numbered from carboxyl carbon (carbon no. 1).
Carbon adjacent to it is carbon number 2 (∝-carbon).
Terminal methyl carbon: ω-carbon or n-carbon.</td><td rowspan="2">Delta Numbering System
Based on the number of carbons, the number of double bonds, and position of double bonds
E.g., linoleic acid is designated as 18: 2: $\Delta^{9, 12}$

(18 carbons, two double bonds, and position of the double bond after C9 and C12 from carboxyl end).</td></tr>
<tr><td colspan="2">Classification</td></tr>
<tr><td colspan="2">Simple Lipids — Esters of FA with alcohol:</td><td>Complex lipids —Esters of FA with alcohol and contain an additional group:</td></tr>
<tr><td>Fats—esters of FA with glycerol.</td><td>Waxes—esters of FA with higher molecular weight alcohols.</td><td rowspan="2"><u>a. Phospholipids</u>

Phosphatidic acid: Esters of FA with alcohol and phosphoric acid residue.

-If alcohol is glycerol: glycerophospholipids (GPL).

-If alcohol is sphingosine: sphingophospholipids.</td></tr>
<tr><td colspan="2">Precursor and Derived Lipids

Include FA, glycerol, steroids, and alcohol.

In addition, derived lipids include ketone bodies, steroids, fatty aldehydes,

Prostaglandins, lipid soluble vitamins, and hormones.

Neutral Lipids.</td></tr>
</table>

b. Glycolipids	***c. Other Complex Lipids***
Glycolipids (glycosphingolipids [GSL]): -Esters of FA, with sphingosine and a carbohydrate.	Sulfolipids, aminolipids, and lipoproteins. Phosphatidic acid: glycerol + 2 acyl residues +PO_4.

Systemic Names of Lipids

Name	***No. Of Carbon Atom***	***Systemic Name***	***Double***
Lauric acid	12	Dodecanoic acid	-
Myristic acid	14	Tetradecanoic acid	-
Palmitic acid	16	Hexadecanoic acid	-
Stearic acid	18	Octadecanoic acid	-
Palmitoleic acid	16	Cis Hexadecenoic acid	1:9 (ω9)
Oleic acid	18	Cis. Octadecenoic acid	1:9 (ω9)
Elaidic acid	18	Trans-octadecenoic acid	1:9 (ω9)
Linoleic acid	18	Cis-9, 12 Octadecadienoic acid	2:9, 12 (ω6)
Linolenic acid	18	Cis-9, 12, 15 Octadecatrienoic acid	3:9, 12, 15 (ω3)
Arachidonic acid	20	Cis 5, 8, 11, 14 Eicosatetraenoic acid	4:5, 8, 11, 14 (ω6)

Unsaturated Fatty Acid		***Isomerism in Unsaturated Fatty Acid***
May contain one or more double bonds		Naturally occurring unsaturated FA has is double bonds.
Monounsaturated	One double bond	

CHAPTER 6

Metabolism of Lipids

LEARNING OBJECTIVES:	**Keywords:**
• Illustrate the assimilation of lipids by the human body. • Explain fatty acid synthesis and degradation. • Explain the metabolism of cholesterol, eicosanoids, ketone bodies and lipoproteins. • Appraise clinical correlation of lipid metabolic disorders.	Alpha and omega oxidation, Beta-oxidation, Cholesterol, Eicosanoids, Ketone bodies, Lipid absorption and digestion, Lipid metabolism syndromes, Lipoproteins, Saturated and unsaturated fatty acid synthesis.

DIGESTION AND ABSORPTION OF LIPID	**Fact file:** Adult human digests 60-150g lipid/day and TAG constitute >90% of intake
Difficulty in the Absorption of Lipids Lipids are hydrophobic TAG too large to be absorbed Digestive enzymes are water soluble	***Solution*** Lipids (including cholesterol) fats absorbed dissolved in lipid micelle Digestive enzymes act at water lipid interfaces

Digestion of Fats: Steps of Digestion

	Location	***Step***	***Enzyme***
1.	*Mouth, stomach: Minor*	TAG → DAG+FFA	Lingual/gastric *lipase*
2.	*Small intestine: Major*	TAG → MAG + FFA CE → Cholesterol + ester PL → FA + LysoPL	Pancreatic *lipase* *Cholesterol esterase* *PLA_2*
3.	*Small intestine lumen:*	Formation of mixed micelle	-

4.	*Intestinal epithelial cells:*	Passive absorption of lipolytic products	-
5.	*Lymphatics:*	Assembly and export of chylomicrons	-

Lipid Absorption:

Site	***Reaction***	***Enzyme***	
Stomach: Gastric lipase	TG ↓ diacyl glycerol+ FA (MCFA)	CE	PL
Small Intestine:	↓	↓	↓
Pancreatic lipase	Sn-1 Sn-2	Cholesterol esterase	PLA_2
Colipase	→	↓	↓
Phospholipid	2MAG	Cholesterol	sn_2 FA
Bile acid	→	+	+
Micelle	IMAG	FA	Lysophosphatidylcholine
	↓ Micelle	bile acid, FA, PL, MAG →	Enteric brush border

Lipid Malabsorption

Defect*:* due to defective intestinal lipolysis or defective mucosal cell metabolism.	Features: Steatorrhea, loss of fat-soluble vitamins in stools.	Causes: Tropical sprue, Non-tropical sprue, Celiac sprue, intestinal lipodystrophy (Whipple's disease).

METABOLISM: Comparison		
	FA Synthesis	**FA Degradation (Oxidation)**
Intermediates	Linked to –SH in proteins (acyl carrier proteins)	Linked to CoASH
Site	Cytosol	Mitochondria
Enzymes	Components of a single peptide	Separate polypeptides
Reducing equivalents	$NADP^+$ / NADPH	NAD^+/NADH
Energy	Requires ATP	Produces ATP
Starts at	Carboxyl end	Methyl end
Carrier	Acyl Carrier protein	CoA
Activation by citrate	Yes	No
Inhibited by palmitate	Yes	No
Acyl/acetyl group carrier	Citrate (into cytosol)	Carnitine (cytosol to mitochondria)
Product	Palmitate	Acetyl CoA
Higher activity	Fed state	Fasting, starvation
Insulin/glucagon	High	Low
Malonyl CoA	Source of two carbon	Not involved

CHAPTER 7

Chemistry of Proteins

LEARNING OBJECTIVES:	**Keywords:**
• Appraise the protein structure and function. • Summarize the properties and classification of amino acids. • Illustrate the classification of proteins. • Identify the diseases related to structural anomalies in proteins.	Amino acids – optical activity, Amphoteric nature, Alpha-helix, Beta-sheet, Diseases related with structural anomalies in proteins, Fibrous and globular proteins, Glycogenic, Ketogenic amino acids, Non- polar, essential, Non-essential, Polar, Primary, Protein misfolding, Proteins, Secondary, Tertiary and quaternary structure of proteins.

PROTEINS: STRUCTURE AND FUNCTION

Functions of Proteins	**Amino Acids**	
Structural: Make up cytoskeleton - Component of collagen, elastin, keratin Enzyme catalysis Transport Storage	Functional units of proteins Composed of: Two functional groups: Amino ($-NH_2$) Carboxyl (-COOH)	**H** **|** **H_2N – C – COOH** **|** **R** Fig. (**7.1**) structure of amino acid: - NH_2 = amino group (basic) - COOH = carboxyl group (acidic) - R = side chain

Hormone Blood coagulation Immunity Control of gene expression	Hydrogen atom (-H) Distinctive side-chain (-R), attached to a central carbon termed *α-carbon.* Except for glycine, all acids contain at least one asymmetric carbon atom (α-carbon atom)	Of these 20 amino acids, only proline is imino acid (-NH-), and not an α-amino acid.

PROPERTIES OF AMINO ACIDS

Optical Activity	**Amphoteric**
Amino acids exhibit optical isomerism: *enantiomers* Two amino acid configurations: D- (dextro or right) and L- (levo or left). **Only L - α-amino acids** occur in proteins	Exist as Zwitter ions in solutions at neutral pH (both positive and negative charges) α-carboxyl group is negatively charged, and α-amino group is positively charged

CLASSIFICATION OF AMINO ACIDS

Based on Structure:	On the basis of the side chain (-R) attached to α-carbon atom:-	**Based on their Metabolic Fate**
Polar (Hydrophilic): Glycine, Serine, Threonine, Cysteine, Arginine, Histidine, Lysine, Aspartate, Asparagine, Glutamate, Glutamine	***Non polar (Hydrophilic):*** Alanine, Leucine, Isoleucine, Valine, Methionine, Proline, Tyrosine, Phenylalanine, Tryptophan	***Glycogenic*** (Ala, Arg, Asp, Cys, Glu, Gly, His, Met, Pro, Ser, Thr, Val) ***Ketogenic*** (Leu) ***Both*** (Ile, Lys, Phe, Trp, Tyr)
Based on Nutritional Requirement		
Essential Amino Acid: Cannot be synthesized by the body and must be supplied in diet - Methionine, Arginine, Threonine, Tryptophan, Valine, Isoleucine, Leucine,	***Non-essential Amino Acid:*** Can be synthesized by the body to meet its demands - Glycine, Alanine, Serine, Cysteine, Aspartate, Asparagine, Glutamate, Glutamine, Tyrosine, Proline	

<table>
<tr><td>Phenylalanine, Lysine, Histidine</td><td></td><td></td></tr>
<tr><td colspan="3">STRUCTURAL ORGANIZATION OF PROTEINS

Two Categories of Proteins</td></tr>
<tr><td colspan="2">*Fibrous proteins*- structural proteins, are more filamentous or elongated

E.g., connective tissue, tender, muscle fibers</td><td colspan="2">*Globular protein* – compactly folded and coated and are water soluble.

They act as transporters.</td></tr>
<tr><td colspan="4">Key levels of proteins are primary, secondary and tertiary structures and quaternary structure</td></tr>
<tr><td>Primary Structure

Synthesized on ribosome as a linear sequence of amino acids in a polypeptide chain.

Determined by the sequence of amino acids.

Serves as a foundation for higher levels of protein structure.</td><td>Secondary Structure

Short segments of polypeptide chain folds to form secondary structure.

Achieved through weak bonds *e.g.*, hydrogen bonding.

Types:
- α helix
- β sheets
- β turn</td><td>Tertiary Structure

Entire 3- dimensional conformation of the polypeptide

Its structure indicates how secondary structure features assemble and relate to each other in 3-dimensional space.</td><td>Quaternary Structure

The structure is formed as a result of interactions between two or more polypeptide chains that give rise to a specific geometry and the aggregate formed is called *oligomer e.g.*, hemoglobin.</td></tr>
<tr><td colspan="2">α HELIX

Cylindrical in shape

Formed by coiling of polypeptide chain on itself at every fourth peptide linkage</td><td colspan="2">β - PLEATED SHEET (or Conformation)

The polypeptide chain is fully stretched out and can fold on itself with its segments packed together.</td></tr>
</table>

CHAPTER 8

Metabolism of Proteins

LEARNING OBJECTIVES:	**Keywords:**
• Describe the assimilation of dietary proteins. • Illustrate the role and regulation of enzymes of protein metabolism. • Identify the disorders of protein metabolism and interpret clinical correlations. • Explain the metabolic fate of amino acids.	Amino acid metabolism, Digestion of proteins, Inherited metabolic disorders and other diseases of protein metabolism, Proteolytic enzyme, Zymogen.

DIGESTION AND ABSORPTION OF DIETARY PROTEINS

Sources of Amino Acids	**Fact File**
Dietary/ Exogenous Proteins*:** Include animal products (meat, poultry, fish and dairy products) and plant products (grains, legumes and vegetables). ***Endogenous Breakdown Protein: Include a breakdown of defective and unneeded cellular proteins. They can be desquamated mucosal cells, digestive enzymes and glycoproteins derived from secretions of salivary glands, stomach, intestine biliary tract and pancreas. Proteins of endogenous origin are digested and absorbed more slowly than that of exogenous origin.	***Dietary Protein Intake*:** 70-100 g/day 50-60% of animal origin 20-30 g in vegetarians ***Proteins Secreted into Intestine*:** 30 g of desquamated cells and 1~2 g plasma proteins, enzymes and mucoprotein Fecal excretion of protein: ~10g/day
Digestion of Proteins	The dietary proteins are cleaved by the action of proteolytic enzymes produced by stomach, pancreas and small intestine

Enzymes for digestion of protein:	Pepsin, trypsin, chymotrypsin, elastase, carboxy peptides, amino peptides.
Digestion of protein begins in the stomach with the action of pepsin:	Produced as inactive zymogen pepsinogen by chief cells Activated to pepsin by H^+ and pepsin itself (auto catalysis) Optimum pH: 2.0
In the small intestine, protein digestion begins by enzymes:	Serine protease Trypsin Chymotrypsin Elastase Carboxy peptidase

Activation of Trypsinogen: Trypsinogen is activated by enterokinase secreted from intestinal brush border in response to secretin and CCK. Once trypsin is formed, it attacks additional molecules of trypsinogen and other zymogens: Chymotrypsinogen, proelastase, procarboxy peptidase to yield active proteolytic enzymes.	***Trypsin:*** Endopeptidase Secreted by intestinal mucosa Hydrolysis of the lysine peptide bond in zymogen: - Releases a small peptide from trypsinogen - Allows molecule to unfold as active trypsin

Enzymes for Digestion of Proteins & Activation of Zymogen form of Proteolytic Enzyme and their Actions:

Zymogen	***Activators***	***Active form***	***Bond specificity***	***Site of action***
Pepsinogen	HCL, pepsin	pepsin	Most amino acid	Stomach
Trypsinogen	Enteropeptidase Trypsin	Trypsin	Basic amino acid	Intestine
Chymotrypsinogen	Trypsin	Chymotrypsin	Aromatic amino acid	Intestine

Proelastase	Trypsin	Elastase	Broad specificity	Intestine
Pro carboxy peptidase	Trypsin	Carboxy-peptidase A, B	Carboxyterminal (exopeptidase) aromatic, neutral amino acid, basic amino acids	Intestine

Digestion in Small Intestine Brush Border	Several peptidases are produced by the brush border of the small intestine and they complete the digestive process.
Enzymes of Small Intestine Brush Border:	Endopeptidase, Exopeptidase, Aminopeptidase, Tripeptidase, Dipeptidase.
Enzyme	***Mechanism of Action***
Carboxy peptidase	Exopeptidase attack carboxy-terminal peptide
Amino peptidase	Exopeptidase attack peptide bond next to the amino terminal.
Tripeptidase	Digest tripeptides to yield dipeptide and free amino acid.
Dipeptidase	Digest dipeptides to free amino acids.
End Products of Protein Digestion	Peptides, dipeptides, tripeptides, and free amino acids

Fate: They get absorbed across the brush border of intestinal mucosal cells. Free amino acids and dipeptides can enter enterocyte by carrier-mediated membrane transport to finally enter the bloodstream.	***Absorption of Amino Acids*** L-isomer of amino acids is actively absorbed by active transport.	***Amino acid transporters present at brush–border:*** **1. *Na – dependent symporters*** **2. *H dependent symporters*:** H-dependent transport is 'E' dependent and may require pyridoxal phosphate.

CHAPTER 9

Intermediary Metabolism

LEARNING OBJECTIVES:	**Keywords:**
• Identify the intermediates that interconnect the metabolic pathways. • Illustrate the inter-organ metabolic pathways and tissue specific pathways. • Explain the metabolism of body fuels and energetics in different organs. • Describe the diseases associated with failure in metabolic integration.	Alpha-keto acids, Fasting, Intermediary metabolism, Obesity, Phosphoenol pyruvate, Starvation and fed state, Sugar phosphates.

The central interconnecting metabolic pathway (pathways of synthesis, degradation, and interconversion of important metabolites) common to most cells and organisms are referred to as intermediary metabolism.

INTERMEDIATES INTERCONNECTING THE MAJOR METABOLIC PATHWAYS:			
Sugar Phosphates: Triose-P Tetrose-P Pentose-P, Hexose-P	**α-Ketoacids:** Pyruvate Oxaloacetate [OAA] α-ketoglutarate [α-KG]	**Coenzyme A (CoA) Derivatives:** Acetyl-CoA Succinyl-CoA	**Phosphoenolpyruvate (PEP)**
Three metabolic key crossroads: Glucose-6-phosphate. Pyruvate Acetyl-CoA.			
Integration of organ metabolism in different physiological states	The co-ordination of metabolic activities of different organs serves to support glucose homeostasis and provides a steady supply of glucose to meet the needs of the brain and RBCs. This also helps in the storage of fuel when available in plenty.		
Three storage forms of fuel	Glycogen, fat and proteins		

Four major tissues with specialized metabolic function	Liver, muscle, adipose tissue and brain. No one tissue can survive metabolically without the other.
Metabolic fuels are used during	***Fed state:*** Fuels used by tissues may be derived from ingested, digested and absorbed food. ***Fasting state:*** Fuels used by tissues are derived from mobilized stores of fuel. ***Starvation:*** Occurs after extended fasting.
Interorgan metabolic pathways	The liver supplies glucose, ketone bodies to other tissues. Adipocytes make FA available to other tissues. The circulatory system transports metabolic fuels, intermediates and waste products among tissues.
Certain metabolic pathways occur in multiple tissues	Cori cycle; Glucose alanine cycle.
Metabolic specialization of organs	Various organs have a different metabolic role and metabolic specialization of organs occur as a result of differential gene expression. All metabolic pathways are under precise regulation to adjust the synthesis and degradation of metabolites to physiological requirements. This is mainly determined by the activity of key enzymes.

Major Organs Involved in the Integration of Metabolism

Organ	***Fuel Storage Pool***	***Mobilized Fuel***	***Conditions***
Liver	Glycogen	Glucose Ketone bodies VLDL-TAG	Fasting, exercise Fasting Fed

Muscle	Glycogen Protein	Lactate Alanine, glutamine	Exercise (intense) Fasting
Adipose	TAG	FFA, glycerol	Fasting (moderate) Exercise

Utilization of Body Fuels in Various Organs

	Liver	***Muscle***	***Adipose***	***Brain***
Function	Maintains blood glucose, makes fat, ketone bodies, stores glycogen	Provides movement: Stores glycogen for its own use; stores proteins.	Manages fat stores	Central control Reliant on glucose for energy
Fed state	Stores glycogen Fat synthesis	Stores glycogen Fat and glucose oxidation Protein synthesis	Stores fat	Uses glucose
Fasting	Glycogen breakdown to make glucose Fat breakdown	Glycogen breakdown Fat Oxidation	Releases stored fat	Uses glucose

ENERGY METABOLISM IN VARIOUS ORGANS

Organ	**Energy Reservoir**	**Preferred Substrate**	**Energy Exported**
Brain	None	Glucose KB (Starvation)	None

CHAPTER 10

Chemistry of Nucleotide

LEARNING OBJECTIVES:	**Keywords:**
• Define the nucleic acid structure and nomenclature. • Describe the biological significance of nucleotide derivatives. • Summarize the role of nucleic acids in our body.	Nucleoside, Nucleotide, Nucleotide derivatives, Purines, Pyrimidine.

NUCLEIC ACID STRUCTURE	
Nucleotide • Combination of heterocyclic amine, a pentose and phosphoric acid. • Monomeric unit of nucleic acids. • Purine and pyrimidines supply building blocks of nucleic acid. • Also, they are high energy intermediates. • Form part of coenzyme: FAD, NAD, NADP, CoA, SAM. • Have regulatory function: signal transduction, second messenger (cAMP, cGMP). • Free nucleotides/ N-bases: Xanthine, hypoxanthine, uric acid.	**The Numbering of Sugars is Primed** ***Nucleoside*** Pentose sugar added to N_9 or N_1 by βN – glycosidic bond ***Nucleotides*** Linking one or more phosphates with a nucleoside onto 5' and of the molecule through esterification

NAMING CONVENTIONS	**Nucleoside**
Nucleotides	Purine: end in 'sine' Adenosine, guanosine

Start with nucleotide name and add mono-, di-, or triphosphate to it. Adenosine monophosphate Deoxythymidine diphosphate		Pyrimidine end in 'dine' Thymidine, cytidine, uridine
Nucleotide		**Function**
1.	***Adenosine Nucleotides***	
	ATP	Source of energy
	cAMP	Second messenger
	Active sulfate *(adenosine 3'phosphate* *5'phospho sulfate PAPS)*	Sulfur donor (proteoglycans) Sulfur conjugation of drugs
	Active methionine *(5-adenosyl methionine SAM)*	Methyl donor, source of propylamine, in polyamines
2.	***Guanosine Derivative***	
	GDP	Coupled to substrate-level phosphorylation
	GTP	Allosteric regulation, energy source
	cGMP	Intracellular signal second messenger (NO)
3.	***Hypoxanthine IMP***	Purine salvage pathway
4.	***Uracil***	Glycogen synthesis
	UDP-G	Glycoprotein synthesis

	UDP-Gln	Glucuronide conjugation reaction of bilirubin, drugs
5.	Cytosine	
	CTP	Phosphoglycerate synthesis
	CDP	CDP choline: formation of sphingomyelin with ceramide
II	***Coenzyme***	NAD, FAD, NADP, CoA, SAM
III	***Monomeric precursors***	Monomeric unit of RNA, DNA

Function	**Example**
Energy Metabolism	ATP, muscle contraction, active transport, ion gradient, phosphate donor
Monomeric Unit	NTP, dNTP (for RNA, DNA)
Physiological Mediators	cAMP, cGMP (second messenger) Signal transduction (GTP binding protein) Adenosine (coronary blood flow)
Precursor Function	GTP (mRNA capping)
Activate Intermediates	UDP-G (glycogen) CDP-choline (phospholipid) SAM (methylation) PAPS (Sulfation)
Allosteric Affects	ATP (negative for PFK) AMP (positive for phosphorylase B) dATP (negative effective RNP reductase)

CHAPTER 11

Nucleotide Metabolism

LEARNING OBJECTIVES:	**Keywords:**
• Describe the pathways of purine and pyrimidine biosynthesis and degradation. • Define the significance and regulation of nucleic acid metabolism. • Correlate the clinical significance of nucleotide metabolic disorders.	*De novo* and salvage pathways, Gout, Lesch Nyhan Syndrome, One-carbon metabolism, OPRT, PRPP, SCID, THF.

FACTS

Characteristic Features of Purines	**Function**
Purine synthesis occurs in the liver. Nitrogenous bases and nucleotides are then transported to other tissues by red blood cells (RBCs). The brain can also synthesize nucleotides. Purines are not metabolized to central metabolites. The ring structure is retained in birds, reptiles, and primates. Other organisms can further breakdown the ring before excretion.	Provides bases (A and G) for energy metabolism and for DNA and RNA synthesis.
	Location
	The cytoplasm of most cells.
	Regulation
	Amidotransferase. Adenosine triphosphate (ATP), guanosine triphosphate (GTP).
Connected to the Following Pathways	***Purine Ring Built-up Using the Following Substances***
Folate metabolism. One-carbon metabolism.	Amino acids glycine, aspartate, glutamine.

Simmi Kharb

Hexose monophosphate (HMP) shunt (*via* phosphoribosyl pyrophosphate [PRPP], ribose)

Deoxyribonucleotides (*via* regulation: PRPP ribonucleotide reductase).

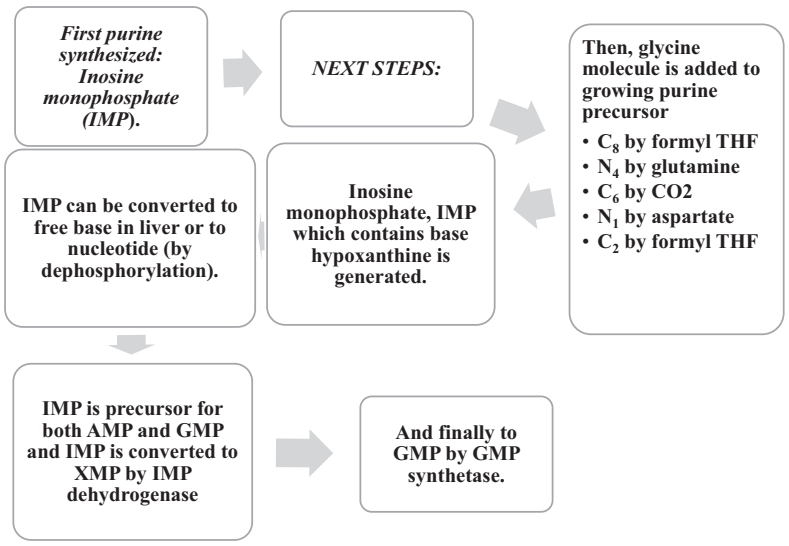


Fig. (11.1). Synthesis of GMP.

Tetrahydrofolate (THF).

CO_2.

Energetics

Require *six molecules of ATP* per purine synthesized.

Precursors

Glycine, ribose-5-phosphate, glutamine, aspartate, CO_2, N10-formyl THF shown in Fig. (**11.1**).

Purine Synthesis	**Salvage**	***De novo***
Synthesis of purines occurs in two ways: Salvage and *de novo*	Activated ribose (PRPP) + base → nucleotide	Activate ribose (PRPP) + A.A. + ATP + CO_2 → nucleotide
	Base is attached	The base is synthesized (require ATP)
	Preformed bases recovered and reconnected to ribose unit	Nucleotide base assembled first then attached to ribose: pyrimidine In purine: base synthesized piece by piece over the ribose-based structure

1st Step:	PRPP (phosphoribosyl pyrophosphate) synthesis Ribose-5-P +ATP —(PRPP synthase)→ PRPP + AMP	PRPP provides ribose moiety to glutamine to form PRA (phosphoribosylamine)
	5 phosphoribosyl -1-pyrophosphate ***Phosphoribosyl aminotransferase*** (Glutamine → Glutamate) 5 phosphoribosylamine (PRA)	*Aminotransferase:* Committed step Important regulated step Inhibit by IMP, GMP, AMP
Next Steps:	Then, the glycine molecule is added to growing purine precursor C_8 by formyl THF. N_4 by glutamine C_6 by CO_2 N_1 by aspartate C_2 by formyl THF Inosine monophosphate, IMP generation (contains base hypoxanthine)	IMP can be converted to a free base in the liver or to the nucleotide (by dephosphorylation). IMP is a precursor for both AMP and GMP and IMP is converted to XMP by IMP dehydrogenase and finally to GMP by GMP synthetase.
Salvage Pathway	• Requires less energy than denovo • Involves ribosylation of free purine • Occurs in the brain, RBC, polymorphs: →	→ Lack APRT: cannot synthesize PRA and utilize exogenous purines to form nucleotides

CHAPTER 12

Molecular Biology

LEARNING OBJECTIVES:	**Keywords:**
• Describe the characteristics, structure, types and functions of DNA and RNA. • Explain cell cycle events and replication of DNA in prokaryotes and eukaryotes. • Appraise process and role of transcription and translation in cells. • Summarize the significance of genetic code and mutations in organisms. • Illustrate the regulation of gene expression. • Identify the basis of cancer and apoptosis.	Apoptosis, Cell cycle, Chargaff's Rule, Cancer, Caspases, DNA, Gene, Mutation, Operons, Oncogene, Polymerases, RNA, Replication, Reverse transcriptase, Ribosomes, Translation, Transcription.

12.1. DNA AND RNA STRUCTURE

Structure of DNA	DNA is composed of a nitrogen base (A, G, C, T) deoxyribose and phosphates.
DNA Double Helix • Double stranded helix with major and minor grooves • Composed of two polynucleotide chains joined by hydrogen bonds between bases • Chains are antiparallel: Chain runs in 5’ to 3’ direction and other in 3’ to 5’ • In the interior of molecule base pairs of strands are stacked (like a spiral staircase)	Four nitrogenous bases: • Purines: A, G • Pyrimidines: C, T • Adenine base pairs with thymine (two bonds) • Guanine base pairs with cytosine (three bonds)
	Base pairing on two strands are complementary:

<table>
<tr><td colspan="2">and phosphate groups are on the outer side of the double helix.</td><td rowspan="2">• PURINE always pairs with PYRIMIDINE
• Adenine on one strand base pairs with thymine on other strands
• Guanine on one strand base pairs to cytosine</td></tr>
<tr><td colspan="2">Chargaff's Rule
- concentration of [A] = [T]; [C] = [G]</td></tr>
<tr><td colspan="3">Structure of RNA</td></tr>
<tr><td colspan="2">RNA is usually a single-stranded molecule.
Three types of RNA namely, mRNA, rRNA and tRNA:</td><td>RNA differs from DNA since RNA contains ribose sugar instead of deoxyribose and uracil (U) rather than thymine.</td></tr>
<tr><td>mRNA
(messenger RNA)</td><td colspan="2">Contains a cap (of methylated GTP) and poly A tails
mRNA is a source of coding information for protein synthesis</td></tr>
<tr><td>rRNA
(ribosomal RNA)</td><td colspan="2">Contains many loops and base-pairing
They are associated with proteins to form ribosomes</td></tr>
<tr><td>tRNA
(transfer RNA)</td><td colspan="2">Act as adaptors that can bind an amino acid at one end and interact with mRNA at other They have a clover leaf structure and contain modified nucleotides
The first loop of clover leaf at 5’ end comprising of dihydrouridine; middle loop contains anticodon which base pairs with a codon in mRNA and third loop are TψC containing both ribothymidine and pseudouridine
At 3’ end, the CCA sequence carries the amino acid</td></tr>
<tr><td colspan="2">REPLICATION</td><td>Cell Cycle Phases</td></tr>
<tr><td>Cell Cycle in Eukaryotes
It is a cell’s lifetime of growth and division (Fig. 12.1).</td><td>S Phase</td><td>• DNA synthesized
• Eukaryotes replicate only once per cell division cycle</td></tr>
</table>

<table>
<tr><td rowspan="2">Regulated by cyclins and kinases.

When cell cycle checkpoints are broken or the cell cycle goes wrong, cells may undergo apoptosis or become cancerous.</td><td></td><td>• Lasts for 8 hrs in humans</td></tr>
<tr><td>G2 and M phase</td><td>• Gap phase G2 occurs before mitosis and cell division (M phase)

• The variable time between two phases</td></tr>
<tr><td rowspan="2">Applied

Paclitaxel (Taxol) prevents cytoskeleton remodeling during cell division: Used in cancers.</td><td>G1 phase</td><td>• Normal cellular functions take place during this phase</td></tr>
<tr><td>G0 phase</td><td>• Resulting phase

• Variable time

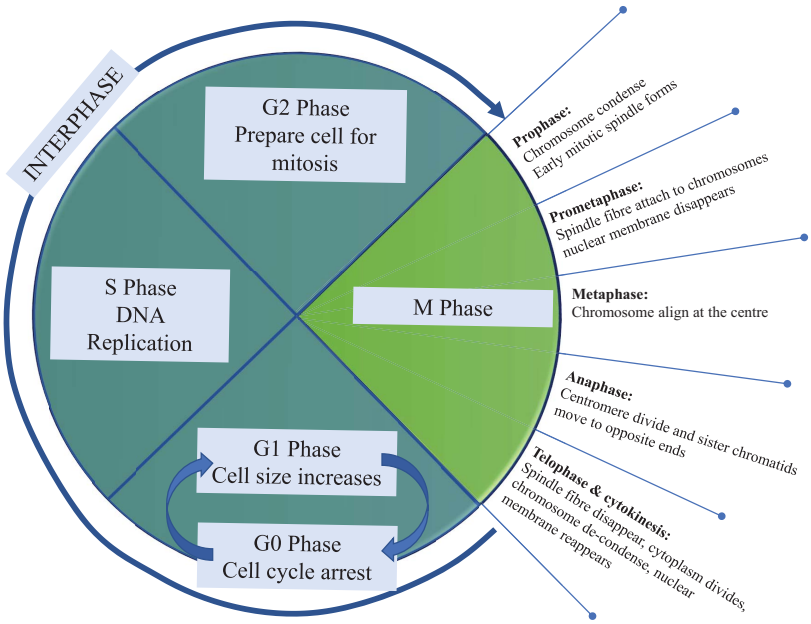
• Tumor cells do not enter the G0 phase</td></tr>
<tr><td>Semi Conservative Replication</td><td colspan="2">Process of making an identical copy of a portion of DNA, using existing DNA as a template for synthesis of new complementary DNA strand</td></tr>
<tr><td colspan="2"> 

Fig. (12.1). Phases of the Cell Cycle.</td><td>Facts

S phase of Interphase

Occurs in a semi-conservative manner

Each strand of ds parental DNA molecule:

- Separates from its complement during replication

- Serves as a template on which a new complementary strand is synthesized</td></tr>
</table>

CHAPTER 13

Genetic Engineering

LEARNING OBJECTIVES:	**Keywords:**
• Describe the tools, techniques and applications of genetic engineering. • Explain the procedures and applications of PCR and cloning.	Cloning, Electrophoresis, PCR, Recombinant DNA Technology, Taq polymerase, Vectors.

MOLECULAR BIOLOGY TECHNIQUES: APPLICATIONS

Recombinant DNA Technology ***Three Basic Approaches***	***Fact File*** A gene might be 1/1,000,000 of genome	
PCR (Polymerase Chain Reaction)	Makes any copies of a specific region of DNA	
Cell-Based Molecular Cloning	Create and isolate a bacterial strain that replicates a copy of the gene of interest	
Hybridization	Make DNA single-stranded. Allow double-stands to reform using a labeled version of the selected gene to make it easy to detect.	
PCR (Polymerase Chain Reaction) (Fig 13.1)	Based on DNA polymerase property of creating a second strand of DNA	
Requirements	Template DNA	Two primers to flank the region to be amplified

Primers	Short (18-30 bases) DNA oligomers complementary to the ends of the region being amplified	
DNA Polymerase	Adds new bases to 3' ends to primer to create a new second strand	
DNA polymerase from *Thermus aquatics*: ***Taq polymerase →***	A bacterium that lives in nearly boiling water in Yellow stone Natural Park Hot springs	Can with strand temperature cycle of PCR that world till DNA pol from *E. coli.*
Uses of PCR	Diagnosis of diseases: - infectious, cancer Forensic medicine Antenatal diagnosis Prenatal sex determination. Paternity contesting	Construction of useful organisms: - Bacteria of biological waste handling, marine spills, nitrogen fixation. Detection of mutations Preimplantation diagnosis of genetic diseases. Anthropology
Advantages of PCR	Rapid Sensitive	Robust Works even with partly degraded DNA
Disadvantages	Only a short region (up to 2kbp) can be amplified.	A limited amount of product is made.
Problems in PCR	Contamination, impurities, improper sample	
PCR Cycle	Based on the cycle of three steps that occur at different temperatures	

<table>
<tr><td colspan="2"></td><td colspan="3">• Each cycle doubles the number of DNA molecules: 25-35 cycles produce enough DNA to be visualized on an electrophoresis gel.

• Each step takes one minute to complete</td></tr>
<tr><td>Steps</td><td><u>Denaturation</u>

Makes DNA single-stranded by heating to 94°C.</td><td><u>Annealing</u>

Hybridize primers to single strands

Temperature around 50°C</td><td><u>Extension</u>

Build second strand with DNA pol and dNTP: 72°C.</td></tr>
<tr><td>Electrophoresis</td><td colspan="3">• Separation of charged molecules in the electric field

• Nucleic acid have one charged phosphate (negative charged) per nucleotide

• Separation based on length: longer molecule moves slower.

• Done in a gel matrix to stabilize: agarose or acrylamide

• Average run: 100 volts across 10cm gel, run for 2 hours

• Stain with ethidium bromide: intercalates with DNA bases and fluoresces orange.

• Run alongside standards of known sizes to get the length.</td></tr>
<tr><td colspan="4">Cloning</td></tr>
<tr><td>Sources of DNA</td><td colspan="3">Genomic DNA: Whole-genome is cut into small pieces and cloned.</td></tr>
<tr><td>Methods</td><td colspan="3">Random shear by

- Partial digestion to generate recognition site at every 256bp by restriction enzyme</td></tr>
</table>

CHAPTER 14

Maintenance of Body Composition

LEARNING OBJECTIVES:	**Keywords:**
• Describe the sources, biological significance and associated disorders of vitamins and minerals. • Explain the regulation and importance of acid-base, water and electrolyte balance in the body. • Identify and define inherited metabolic disorders. • Categorize xenobiotics and provide their significance. • Illustrate the mechanisms of oxidative stress and antioxidant defences.	Acids, Antioxidants, Bases, Buffers, Deficiency diseases, Dehydration, Electrolytes, Free radicals, Genetic screening, ICF and ECF, IMD, Minerals, pI, pH, ROS, Vitamins,Water, Xenobiotics.

VITAMINS

Sources, Active Form and Importance of Various Vitamins

	Pro Vitamin (Source)	***Active Form***	***Metabolic Importance***
	Fat- soluble Vitamins		
1.	*Vitamin A:*		
	β carotene (vegetable fruit) ↓	Retinal Retinol Retinoic acid	Visual pigment (vision) Coenzyme (sugar transport) Signal molecule (development and differentiation)
	Retinol (Milk, liver, egg yolk)		
2.	Vitamin D	Calcitriol	Hormone

	(Cholesterol → Cholecalciferol (Cod liver oil, milk, egg yolk) ↓ Calcitriol		(Calcium metabolism)
3.	Vitamin E: Tocopherols (Cereals, liver, egg, oil seeds)	Tocopherols	Reducing agent (antioxidant)
4.	Vitamin K: Phylloquinones (Intestinal bacteria, vegetables, liver)	Phylloquinones	Blood clotting
	Water- soluble Vitamins		
	Vitamin B complex:		
5.	Thiamin (grain, yeast)	Thiamin diphosphate (TDP)	Transfer of hydroxyalkyl residues
6.	Riboflavin (milk, egg)	FMN, FAD	Hydrogen transfer
7	Nicotinate, nicotinamide (Meat, yeast, fruit, vegetable)	NAD, NADP	Hydride transfer
8.	Pantothenate (wide distribution)	CoA	Activation of carboxylic acid
9.	Pyridoxal, pyridoxol, pyridoxamine (Meat, vegetable, grains)	PLP (pyridoxal phosphate)	Activation of amino acids

10.	Cobalamin (Meat, liver, egg, milk)	5-deoxy adenosyl cobalamin Methyl cobalamin	Isomerization
11	Biotin (yeast)	Biotin	Transfer of carboxyl groups
	Other Water-soluble Vitamins		
12	Ascorbic acid (Fruit, vegetables)	Ascorbate	Stabilization of enzyme systems, coenzyme, antioxidant.

Fat-Soluble Vitamin: Function and Deficiencies

	Pro Vitamin	***Functional or Active Form***	***Metabolic Importance***	***Features of Deficiency***
1.	Vitamin A Beta carotene Retinol	Retinal Retinol Retinoic acid	Visual pigment (vision) Coenzyme (sugar transport) Signal molecule (development and differentiation)	Defective night vision or night blindness Keratinization of epithelium: Cornea Lungs Conjunctiva GIT Genitourinary tract Bitot's spots Xerophthalmia Blindness Increased susceptibility to infections

CHAPTER 15

Clinical Biochemistry, Physiology & Genetic Disorders

LEARNING OBJECTIVES:	Keywords:
• Explain the biochemistry of blood, its functions and associated disorders. • Illustrate the concepts of immunology, constituents and diseases of the immune system. • Describe the biochemical basis of structure and functions of muscle, nerves and eye. • Identify and interpret organ function tests. • Define and diagnose genetic disorders.	Action Potential, Antibody, Antigens, Blood, Clotting factors, Calcium, Genetic disorders, Homeostasis, Immunity, Immunoglobulins, Jaundice, Kidney, Lens, LFT, Mucin, Neurons, Platelets, Sarcomere, Tear, Vaccines.

15.1. BLOOD

<table>
<tr><th>Biochemistry of Blood</th><th colspan="3">Blood Performs Three Major Functions (Fig. 15.2)</th></tr>
<tr><td>Composition of Blood (Fig. 15.1)</td><td colspan="2">Transport</td><td>Defense</td></tr>
<tr><td rowspan="4">8% of the body weight (5–6 L)

Suspension of cells in carrier fluid:
Water (90%)
Proteins (7%)
Inorganic (1%)
Organic (2%)
Plasma: 55%

Leucocytes and platelets: 2%</td><td>Oxygen and carbon dioxide

Food molecules (glucose, lipids, amino acids)</td><td>Ions (e.g., Na^{+}, Ca^{2+}, HCO^{3-})

Wastes (e.g., urea)

Hormones</td><td>Defending the body against infections or other harmful foreign materials.

All types of WBCs participate in the body’s defence mechanism.</td></tr>
<tr><td colspan="3">Homeostatic Functions</td></tr>
<tr><td colspan="2">Heat

Water- salt balance

Acid-base balance</td><td>Osmosis

Blood clotting

Formation of hormones</td></tr>
</table>

<table>
<tr><td>Erythrocytes: 43%</td><td></td><td></td></tr>
<tr><td>Red Blood Cells (Erythrocytes)</td><td>Does not contain nucleus, chromatin

Does not contain mitochondria</td><td>ATP produced from anaerobic glycolysis mainly and ends in lactate (~90%).</td></tr>
<tr><td colspan="2">Structure

In an adult human, hemoglobin (Hb) molecule comprises of four polypeptides

Two alpha (α) chains consisting of 141 amino acids

Two beta (β) chains consisting of 146 amino acids

Each of these chains is attached to the prosthetic heme group.

One Fe-atom is present at the center of each heme group.

One O_2 molecule binds to each heme group.

It is a reversible reaction.</td><td>Glycolysis in RBCs has the Following Features

2,3 BPG will be produced and not 1,3 BPG.

2,3 BPG binds O_2 to hemoglobin:

Low concentration of 2,3 BPG will increase affinity hemoglobin (Hb) to O_2

PPP is the main pathway for producing of reductive equivalents NADPH

It is accountable for transporting O_2 and CO_2.</td></tr>
<tr><td colspan="3">Diseases Associated with the Inadequate Synthesis of Hemoglobin Components</td></tr>
<tr><td>Porphyria</td><td>Thalassemia</td><td>Iron deficiency anemia</td></tr>
</table>

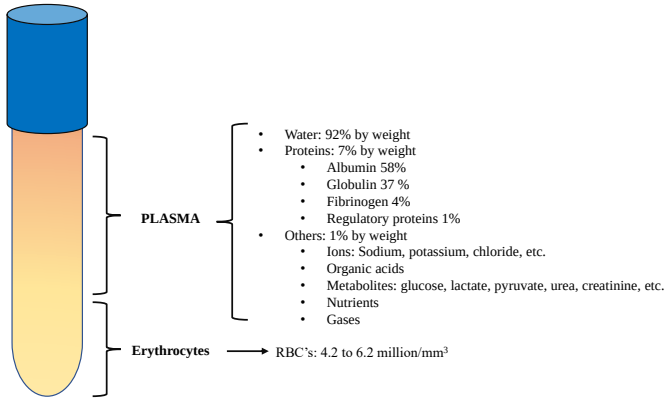


Fig. (15.1). Composition of Blood.

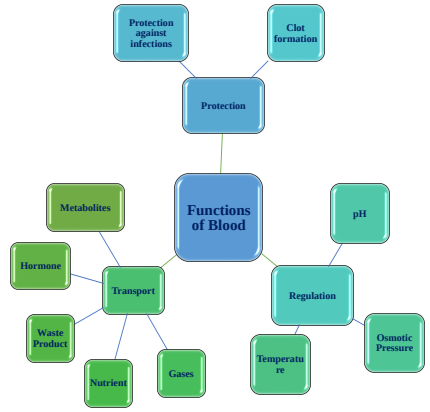


Fig. (15.2). Functions of Blood.

Normal proteins levels: 65-85 g/l

Albumins: 35-50 g/l.

Fibrinogen: 2-4 g/l.

Globulins:

α1 globulins: 1-4 g/l

α2 globulins: 4-8 g/l

β globulins: 6-12 g/l

γ globulins: 8-16 g/l

Hemostasis	**Vascular Constriction**
Definition: Inhibition of loss of blood due to broken blood vessel • Achieved by several mechanisms: • Vascular constriction • Platelet plug formation • Blood coagulation	Damage to blood vessel wall causes the contraction of smooth muscle which results from: • Myogenic local spasm • Factors/ chemicals released from the damaged tissues & blood platelets • Reflexes of the nervous system

CHAPTER 16

The Endocrine System

LEARNING OBJECTIVES:	**Keywords:**
• Explain the synthesis, biological significance and diseases of hormones.	Adreno-corticoids, Catecholamines, Growth hormone, Para-thyroid, Thyroid.

GH (GROWTH HORMONE)	
Fact File: GH • 19 residue polypeptide • Produced by the anterior pituitary. • Stimulates growth and metabolism in muscles, bone and cartilage cells. • Acts indirectly via growth factors (produced by the liver following its stimulation). • GH is an anabolic hormone, it stimulates protein synthesis in bone and muscle.	GH is also called somatotropin and is secreted by the anterior pituitary. The secretion of GH is mediated by two hypothalamic hormones: growth hormone-releasing hormone (HRH) and somatostatin (growth hormone inhibiting hormone). **Synthesis of GH** GH is synthesized in somatotrophs (a subclass of acidophilic cells) in the anterior pituitary gland. It is also called somatotrophin. It stimulates the production of growth factors IGF (insulin-like growth factors) in the liver. Release of GH from the pituitary is stimulated by GHRH (GH releasing hormones) and inhibited by somatostatin (SS) It is released in pulses.

Metabolic Effects of GH		
	Decrease	*Increase*

Carbohydrate metabolism	Glucose uptake in extrahepatic tissues Insulin sensitivity	Hepatic glucose output hepatic glycogen stores Plasma glucose
Lipid metabolism	-	Lipolysis Plasma FFA Plasma ketone bodies
Protein metabolism	Nitrogen excretion	Amino acid uptake Protein synthesis

GH Disorder ***GH Deficiency*** It occurs both in children and adults. In children, it can be familial or may be due to tumors (cranio-pharyngioma). In adults, it is as a result of structural or functional abnormalities of pituitary.	***Manifestations*** In children, there is growth failure. In adults, GH deficiency occurs in case of partial or complete failure of the anterior pituitary. Symptoms include fatigue, loss of motivation, diminished feeling of well-being even social withdrawal, osteoporosis and alteration in body composition.
GH deficiency causes a condition called dwarfism. If GH is produced in excess before bone growth stops, a person is taller than normal. This condition is called gigantism. If excess GH is released in an adult, acromegaly results. Bones cannot elongate in acromegaly, soft tissue enlargement occurs namely skin, muscle, hands, feet, nose, ears, tongue and chin.	
Acromegaly	
Cause	Pathologic GH excess Autonomous GH excess
Pathology	Pituitary tumor

	Ectopic production of GHRH or GH.
Features	Progressive enlargement of hands, feet, facial bones (including mandible, skill), coarsening of facial features. Hypertension, accelerated atherosclerosis, proximal muscle weakness, sleep apnoea, increased risk of insulin resistance/diabetes. Organomegaly is common. Excessive sweating or heat intolerance. Local effects of the tumor (headache or visual complaints) or symptoms related to other anterior pituitary hormones. Features of co-secretion of prolactin are seen in 40% of patients of acromegaly.
Thyroid Glands: Functions of Thyroid Hormone	
1. Calorigenesis:	Thyroid hormones generate heat by stimulating mitochondrial O_2 consumption and the production of ATP required for Na pump.
2. Carbohydrate and fat metabolism: (i) Carbohydrate	*Catabolic action* • Stimulate intestinal absorption of glucose • Stimulate hepatic glycogenolysis • Potentiate glycogenolytic actions of epinephrine • Stimulate insulin breakdown
(ii) Lipid:	• Lipolytic- Direct action • Indirect action via potentiating action of other hormones like: GC glucagon, GH, epinephrine. • Increase the oxidation of FFA. • Decreased plasma cholesterol by: inhibition of bile acid formation in the liver.

SUBJECT INDEX

A

Abetalipoproteinemia 111, 227
  rare genetic disorder 111
Acetyl CoA carboxylase (ACC) 46, 104, 107, 248
Acid 11, 16, 21, 33, 34, 45, 59, 60, 69, 71, 76, 88, 89, 91, 94, 97, 98, 99, 100, 106, 114, 115, 119, 121, 123, 129, 131, 132, 133, 134, 135, 139, 142, 144, 150, 153, 161, 224, 258, 261, 263, 269, 270, 276, 277, 280, 281, 313, 316, 324, 327, 329, 339
  arachidonic 21, 89, 114, 115
  ascorbic 76, 99, 106, 224, 280, 281, 313, 316
  benzoic 134
  deoxyribonucleic 278
  free fatty (FFA) 94, 100, 106, 150, 339
  glucogenic amino 132
  glucuronic 59, 60, 76, 269
  glutamic 123, 270
  hexadecanoic 88, 89
  hippuric 134
  homogentisic 142, 329
  hyaluronic 316
  hydroxylase phytanic 98
  hypochlorous 276
  imino 121, 129
  keto 33, 131, 133, 134, 139, 261
  lactic 34
  linolenic 16, 89, 91, 100
  lipoic 45, 69, 71
  lysophosphatidic 115
  methylmalonic 135
  myristic 89
  oleic 89
  palmitic 88, 89, 119
  phenylacetic 134
  phosphatidic 88, 89, 91
  phosphoric 153
  polyenoic 97
  pyroglutamic 135, 258
  stearic 16, 89, 91
  uric 11, 161, 263, 277, 324, 327
  xanthurenic 144
Acidosis 140, 141, 231, 235, 236, 237, 256, 329, 335
  lactic 256, 329
  renal tubular 231, 237
  respiratory 235, 236
Acne 348
ACS Acyl CoA synthase 105
Activator 49, 77, 127, 201, 242, 248, 266, 288
  allosteric 49
  tissue plasminogen 288
Addison's disease 347, 354
Adenosine deaminase (ADA) 161, 163
Adenosyl methionine enzyme 271
ADP Adenylate kinase 160
Adrenal 349, 350
  carcinoma 350
  failure 349
  function tests 350
Aging 198, 278, 334
  premature 198
  premature skin 334
  process 278
Alanine 49, 51
  racemase 49
  transaminase 51
Alkaline phosphatase (ALP) 47, 50, 51, 52, 242, 246, 248, 323
Alkaptonuria 133, 140, 142, 145, 261, 329
Allergic disease 297
Alzheimer's disease 249, 329
Aminotransferase 159
Ammonia 134, 144, 146, 321, 267
  levels 134, 146, 267
Anaplerotic reactions 73, 80
Anemia 50, 51 69, 70, 71, 75, 225, 237, 241, 283, 286, 328, 331
  hemolytic 69, 70, 71, 75, 225, 283
  iron deficiency 286
  megaloblastic 51
  post gastrectomy 241

sickle cell 328
Anthropology 216
Antioxidant 248, 276, 278, 319
depletion 278
glutathione 319
nutrients 276
property 248
Apoptosis 10, 169, 171, 206, 207, 208, 209, 210, 211, 213, 214
and cancer 213, 214
ATP 12, 25, 34, 38, 40, 41, 42, 43, 46, 74, 75, 76, 103, 129, 304, 339
moles of 42, 43, 74, 103, 129
generation TCA cycle 12
hydrolysis 25, 34, 46, 304
pathways 75
production 41, 76, 339
synthase 38, 40, 41, 42, 43
ATP synthesis 33, 43
energy 43
Autoimmune disease(s) 276, 278, 297, 352
atherosclerosis 278
Autolysis 320
Autolyzed lenses 320
Autosomal dominant 111, 328
disorder 111
X-linked inheritance 328
Autosomal recessive disorder 163, 245

B

Bacterial inhibition assays 135, 258
Biochemical screening tests 134
Biologic effects of glucocorticoids 346
Blood coagulation 121, 290
immunity 121
tests 290
Blood flow 83, 113, 155, 229, 325
coronary 155
decreased renal 229
stop 113
Blood glucose 82, 83, 85, 150, 152, 346
high 83
levels 82, 85, 346
Blood pressure 113, 230, 329, 340, 345
high 113, 329
Blood spot assay 135, 259
Blood urea 325

C

Cancer 9, 45, 50, 169, 171, 178, 202, 205, 207, 213, 214, 276, 278
cells liberate cathepsins 9
colon 205, 207
pancreatic 207
prostate 207
CAP-binding protein (CBP) 192
Carbamoyl phosphate synthase deficiency 256
Carbamoyl phosphate synthetase 164
Carbohydrate 64, 65
absorption 65
storage 64
Cardiovascular diseases 278, 320, 330
Caspase activated DNase (CAD) 164, 209
Chemiosmotic theory 43
Cholesterol 105, 248
biosynthesis 248
fat oxidation 105
Cholesterol synthesis 12, 103, 104, 109, 255, 256, 257
defects 255
Cholinesterase 45
Chymotrypsin 127
serine protease trypsin 127
Cirrhosis 242, 245, 247, 321, 322, 331
hepatic 245
Collagenase 9, 10
Collagen 60, 244, 316, 330, 346
fibers 60, 316
formation 244
synthesis 330, 346
Colon cancer NYCN Neuroblastoma 205
Colorectal cancer 50, 179
hereditary nonpolyposis 179
Copper deficiency 281
Coris disease 77
Creatine metabolism defects 256
Cystathione synthase 137
Cystathionine beta syntheses 259
Cystic fibrosis 26, 27, 227, 262, 263, 328, 329
trans membrane conductance regulator 26
transmembrane regulator (CFTR) 26, 329
Cystinosis 137
Cystinuria cystinosis 139
Cytathioninuria 138

D

Dementia 225, 249, 329, 332
Diseases 26, 45, 64, 77, 111, 114, 120, 123, 130, 216, 227, 228, 229, 237, 244, 257, 258, 261, 274, 275, 276, 277, 278, 300, 301, 315, 318, 320, 321, 322, 328
  acute life-threatening 258
  cardiac Neurodegenerative 278
  celiac 130, 244
  cholestatic liver 227
  chronic liver 321, 322
  chronic obstructive airway 237
  chronic systemic 315, 318, 320
  coronary artery 276
  debranching enzyme Anderson's 77
  genetic 216, 261
  immune 297
  metabolic 64, 274
  peripheral vascular 114
  premature coronary 111
  sickle cell 123, 328
Disorders 29, 35, 130, 146, 151, 207, 238, 241, 254, 255, 258, 260, 265, 266, 267, 285, 297, 298, 328
  ammonia detoxification 151
  ferrous state 241
  genetic 285, 328
  glycogen storage 260, 267
  lymphoproliferative 166
  lysosomal storage 255, 265
  neurodegenerative 207
  of carbohydrate metabolism and transport 151
  of fatty acid oxidation 151
  of hypercalcemia 238
  of immune regulation 297
  of ketogenesis 151
  of protein absorption 130
  peroxisomal 255, 267
  progressive degenerative 258
DNA 6, 7, 169, 172, 173, 175, 176, 177, 201, 209, 212, 213, 216, 217, 218, 219, 221, 263, 278, 280
  binding proteins 213
  copy of mRNA 218
  double helix 169
  expression 7
  finger printing 221
  foot printing 221
  fragmentation 209
  fragments 173
  genomic DNA 217
  gyrase 176
  helicases 172
  in prokaryotes and eukaryotes 169
  ligase 172, 176, 218, 219
  methylating enzymes 201
  of maternal origin 6
  oligomers complementary 216
  polymerases 172, 173, 176, 177, 212, 216
  primase enzyme 172
  repair enzymes 278, 280
  sensors 263
  synthesis 172, 175
  telomerase 177
DNA and RNA 157, 164, 213
  polymerase 213
  synthesis 157, 164
DNA damage 174, 177, 179, 207, 279
  repair 207
DNA replication 11, 173, 174, 175, 178, 212, 213, 242
  and RNA synthesis 242
  and transcription 213
  errors 178
  transcription 11
Down syndrome 264

E

Electroencephalography 263
Electron-transport heme proteins 270
Electrophoresis 215, 217, 296
  gel 217
Endergonic reaction 35
Endothelial derived-relaxing factor (EDRF) 277
Enoyl reductase 101
Enzyme(s) 53, 107, 108, 127, 262
  acetyl CoA carboxylase 107
  assay Leukocyte 262
  for digestion of proteins 127
  suicidal 53
  thiolase 108
Epilepsy 255, 258, 329, 332
  myoclonic 255, 329, 332
Euphoria depression psychosis 349

F

Fabry's disease 265
Familial hypercholesterolemia (FH) 111, 113
Fasting blood sugar (FBS) 83
FA synthases 101
Fatty acid 98, 100, 102, 106, 107
  oxidation results 98
  synthase (FAS) 100, 102, 106, 107
Fibroblast growth factor receptor 329
Focal adhesion kinases (FAK) 209
Functions, renal 325

G

Galactokinase 77
Galactosemia 77, 259, 265
Galactosidase 200
Gastrectomy 241
Gastric 95, 323, 324
  function tests 323
  lipase 95
  ulcer 324
Gaucher disease 265
Gierke's disease 84
Gilbert's syndrome 76
Glomerular filtration rate (GFR) 324, 325, 326, 336
Glucokinase gene 68
Gluconeogenesis 33, 34, 64, 79, 84, 255, 341
Glycogen 3, 12, 56, 64, 67, 74, 76, 81, 82, 85, 149, 151, 155
  protein synthesis glycolysis 12
  pyruvate kinase 81
Glycogenesis 74, 81, 86
Glycogenolysis 34, 81, 86, 339
  hepatic 339
Glycogen 73, 81, 84, 154
  synthase 73, 81
  synthesis 84, 154
Glycolysis 33, 37, 64, 67, 70, 71, 76, 77, 80, 81, 84, 85, 286
  anaerobic 70, 286
Glycolytic pathway 131
Glycosidase enzyme 312

H

Hartnup disease 26, 130, 136, 225, 267
  symptoms in intestine and kidney 26
Hashimoto's disease 352
Hematopoietic cell transplantation (HCT) 267
Heme proteins 40, 52
Hemochromatosis 257, 328, 331
Hemoglobin components 286
Hemolysis 77, 229, 231, 239, 281, 322, 331
  increased 331
  ineffective 322
  oxidative 281
Hemorrhagic disease 225
Hemosiderosis 241, 281
Hereditary non polyposis colorectal cancer (HNPCC) 178, 179
Hexokinase enzymes 71
Hexosaminidase 262
Homocystine 137
Homocystinuria 134, 137, 255, 262, 266
  methylmalonic academia 266
  muscular dystrophy Serum methionine 262
Homogentisate oxidase 140, 142, 261
  deficiency 140, 142, 261
Homogentisic acid oxidase 329
Hookworm infection 241
Hormone(s) 5, 59, 81, 87, 104, 222, 225, 252, 282, 285, 287, 288, 324, 328, 337, 339, 340, 353, 354
  adrenal cortex 354
  anterior pituitary 339
  hypothalamic 337
  mineralocorticoid 340
  polypeptide 5
  regulating carbohydrate metabolism 81
  releasing hormone (HRH) 337
  sensitive lipase (HSL) 104
  steroid 87, 252
Human alpha glucosidase enzyme 265
Huntington's disease 123, 197, 328
Hurler's Disease 11
Hydrolases 8, 46
Hydrolysis 21, 54, 74, 127, 304
  intestinal mucosa 127
  of ATP by myosin and conformation change 304
Hydrolytic reaction 46
Hydroperoxidase 37
Hydroperoxy eicotetraenoic acid 115
Hydrophobic 4, 14, 18, 22, 87, 94
Hyperargininemia 137
Hypercalcemia 238, 281, 327

Hypercalciuria 349
Hyperglycemia 83, 349
Hyperkalemia 231, 281
Hyperlipidemia 113, 114
Hyperplasia 348
Hyperprolinemia 133
Hypertension 113, 143, 339, 343
Hyperthyroidism 238, 352
Hyperuricemia 267

I

Immune 277, 297
  regulation 297
  response neurotransmitter 277
Immune response 291, 292, 293, 300
  adaptive 291
Immunity 285, 291, 292, 294, 295, 296, 300
  adaptive 291, 292, 300
  humoral 300
  innate inborn 291
  passive 295
Immunodeficiency 297
Immunoglobulin biosynthesis 297
Immunological memory 292, 300
Immunologic dysfunction 297
Inborn errors phenylketonuria screening Tests 261
Infections 66, 83, 113, 163, 224, 244, 247, 267, 278, 285, 287, 291, 298, 300, 312, 347
  adrenoleukodystropy 347
  bacterial 312
  cholera 66
  protozoal 163
  recurrent pulmonary 298
Inherited autosomal recessive 241
Inherited 65, 126, 133, 139, 141, 146, 222, 254, 257, 262, 328, 350
  lactase deficiency cramps 65
  Metabolic Defects 350
  metabolic diseases 257
  metabolic disorders (IMD) 126, 133, 139, 141, 146, 222, 254, 257, 262
  single gene disorders 328
Innate immune 292, 300
  response 300
  system 292
Insulin 4, 5, 76, 78, 79, 81, 82, 83, 104, 107, 109, 151, 246, 253, 338, 347
  resistance 82, 151
  secretion 246, 347
  sensitivity 338
Ischemia reperfusion injury 278

K

Keshan's disease 251
Ketoacidosis 97, 237
  diabetes mellitus ketone body production 97
  diabetic 231
Ketogenesis 151, 340
Ketogenic amino acid 120, 132
Ketoglutarate dehydrogenase 225
Ketone body 108
  synthesis 108
  utilization 108
Ketonuria 336
Kidney 51, 83, 239, 241, 333
  damage 83
  disease 51, 241
  failure 333
  stones 239
Klinefelter syndrome 329, 332
Kreb's cycle 79, 99
Kyphosis 227, 249

L

Lactacidemia 41
Lactacidosis 41, 237
Lactate dehydrogenase (LDH) 14, 46, 51, 70, 246
Leprosy 297
Lesch nyhan syndrome 157, 163, 167
Lipid 94, 280
  metabolism syndromes 94
  oxidation reaction 280
Lipoprotein lipase deficiency 112
Lipoxygenase 115
Liver 247, 251, 262, 275, 289, 320, 321
  cirrhosis 247, 320
  diseases 289
  function tests 262, 321
  kidney bile urine 275
  necrosis 251
Long terminal repeats (LTRs) 199
LP in human disease 111

Lung 253, 329
damage 253
infections 329
Lysosomal 10, 137, 258, 267, 331
disorder 137, 258
storage disease 10, 267, 331
Lysosomes 4, 8, 9, 10, 11, 12, 13, 26, 29, 77, 254
heterophagy 9
macrophage 10

M

Macromolecular synthesis anabolic products 32
Magnesium deficiency 243
Maple syrup urine disease (MSUD) 136, 139, 144, 145, 255, 258, 261, 263, 265
Mass spectrometry 262
Mastocytosis 205
Maternal 5, 264, 332
Inheritance 5
plasma screening 264
transmission 332
McArdle disease 260
McArdle's syndrome 77
Megakaryocytes 288
Megaloblastic anaemia 226, 282
intrinsic factor 226
Menke's disease 245
Menkes disorder 257
Metabolic disorders 94, 126, 133, 135, 146, 157, 222, 254
inherited 126, 133, 146, 222, 254
Methionine synthase 226
Methyl malonyl CoA mutase 140, 226
Mitochondrial 255, 266, 329
disorders 255, 266
genetic inheritance disorders 329
Mitochondria signal transduction 276
Monooxygenases 75, 99, 106, 109, 268, 274
Monophosphate decarboxylase 164
Mucosal block theory 240
Muscle 51, 77, 260
disease 51
glycogenosis 260
phosphorylase 77
Myeloperoxidase 277
Myocardial 50, 51, 244
fibrosis 244
infarction 50, 51
Myoclonic epilepsy with ragged red fibers (MERRF) 329, 332
Myometrial contraction luteolysis 116
Myotonic dystrophy 332

N

Natriuresis 116, 229
Neoplastic transformation 203
Nephrocalcinosis 137
Nephropathy 83
Nerve cell action potentials and synaptic transmission 307
Nervous 92, 116
system vasodilation 116
tissue ganglioside 92
Neurofibromatosis 332
Neurological 41, 163, 225, 250, 258
abnormalities 41, 250
symptoms 163, 225, 258
Nicotinic acid 267
Non-Hodgkin's lymphoma topoisomerase II 50
Non-insulin dependent DM (NIDDM) 82
Non-ketotic hyperglycemia (NKH) 259, 263
Nucleoside phosphorylase 160

O

Oncogenes encode proteins 204
Ophthalmoplegia 225, 258
Oral 66, 83
glucose tolerance test (OGTT) 83
hydration therapy 66
Organ function tests liver 320
Orotic acid 163, 167, 262
urea 167
Osmotic lysis 30
Osteoarthritis 58
Osteoclastic bone resorption 344
Osteoporosis 338
Osteosclerosis 249
Oxalate urolithiasis 137
Oxidase 13, 37, 39, 40, 42, 244, 253
copper aldehyde 253
mono amine 244
Oxidation 40, 46, 67, 98, 350
of iodide 350

of LCFA 98
reaction 40, 67
reduction reaction 46
Oxidative 37, 72, 79, 144, 222, 276, 277, 278, 279
damage of molecules cells 276
damage of ROS 279
decarboxylation 72, 79, 144
phosphosporylation 37
stress 222, 276, 277, 278, 279
Oxygenase 37

P

Pancreas hepatitis 50
Pancreatic lipase 94, 95, 110, 117
cholesterol 94
Pancreatitis 52
Paralysis, respiratory 243
Parkinson's disease 142
Pathogenesis 274, 278
Pathway(s) 33, 64, 67, 71, 72, 73, 74, 75, 76, 77, 81, 115, 146, 148, 154, 164, 165, 166, 167, 254, 257, 318
carbohydrate 75
catabolic 33, 64
central interconnecting metabolic 148
cytoplasmic 67
for digestion of carbohydrates 64
interrelated biochemical 254
of eicosanoid metabolism 115
oxidative 75
pentose phosphate 33, 257
protein degradation 146
purine salvage 154, 167
signal transduction 318
Peptic ulcer 50, 241
PG G/H synthase (PGS) 115
Phosphatidyl 18, 91, 211
ethanolamine (PE) 18, 91
serine (PS) 18, 211
Phosphoglycerate synthesis 155
Ping pong mechanism 24
Pinocytosis 25
Plasminogen 288
Platelet 116, 277, 287, 288, 341
aggregation 116, 277, 288, 341
derived growth factor (PDGF) 288
plug formation 287
Polymerase chain reaction 215
Polymerases 169
Polysaccharide hydrolyzing enzyme 8
Pompe's disease 77, 265
Post transcriptional modifications 212
PPi hydrolysis 34
Proapoptotic protease 208
Processed cheese 249
Production 97, 207
of ketone bodies in excess 97
of TP53 tumor suppressor gene 207
Programmed cell death (PCD) 208
Prostanoid synthesis 99
Prostatic Cancer 50, 52
Protein(s) 6, 8, 16, 20, 21, 23, 24, 27, 28, 59, 110, 120, 122, 123, 128, 135, 140, 146, 172, 194, 200, 201, 209, 260, 265, 273, 281, 288, 291, 292, 302, 307, 316, 332
antimicrobial 292
carrier in lipid bilayer associates 24
coagulants 288
conformation 123
damage liver 273
dependent activator 200, 201
digestion peptides 128
endocytosed 8
folding 194
excessive 140
globular 23, 59, 120, 122, 302
immunoglobulin 291
inhibitors 146
insoluble 316
integral 16, 20, 21, 28, 307
involved in DNA synthesis 172
kinases 209
lysosomal associated membrane 260
metabolism defect 135
microfibril-forming 332
moiety 110
oxidation 281
phosphatases dephosphorylate 194
porin 20
restriction 265
synthesis transport system 6
tetramer transmembrane 27
Proteolysis 194, 342, 351
Proteolytic enzyme 126, 127
Prothrombin 194, 289
activator 289
Protooncogenes 204, 205, 342
PRPP synthase 159

Pyruvate 33, 46, 67, 70, 71, 72, 73, 78, 79, 80, 81, 132, 225, 248, 255, 287, 312
carboxylase 73, 79, 80, 248, 255
dehydrogenase 71, 72, 255
glutamine synthetase 46
kinase (PK) 70, 71, 78, 81

R

Rate of glycolysis 71
RBC 19, 111
and cornea of eye 111
plasma membrane 19
Reactions 7, 62, 100, 106, 124, 146, 155, 268, 270, 273, 300
enzymes catalyze 268
glucuronide conjugation 155
hepatitis 273
immune 300
mono oxygenase 270
of fatty acid synthesis 100, 106
of monosaccharides 62
oxidative 7
protein color 124
transmethylation 146
Reactive 179, 222, 274, 276, 277, 278, 279, 283
oxygen species (ROS) 179, 222, 276, 277, 278, 279, 283
species of xenobiotics 274
Recombinant DNA technology 215
Reductase isomerase 115
Refsum disease 98
Renal 137, 237, 238, 239, 243, 245, 262, 326, 333, 349
artery stenosis 349
diseases 326, 333
failure 137, 237, 238, 239, 243
function test 262
tubular absorption defects 245
Renal transport defect 136, 138
of cysteine amino acid 138
of tryptophan and neutral amino acid 136
Repressor 200, 201
protein changes 200
Respiratory 2, 38
chain enzymes 38
enzymes 2
Retina 83, 226, 317, 318, 319
cataract 83
Retinol binding protein 327
Reverse transcriptase 169, 177, 218
RNA 7, 13, 155, 169, 170, 172, 175, 176, 179, 180, 185, 199, 212, 213, 219
human genome transcribes 199
interference 199
primers 175, 176
ribosomal 170, 179
RNA polymerase 7, 49, 180, 185, 188, 191, 213, 246
and transcription factors 191
dependent 246
Role 119, 246, 250, 274, 279, 316
in biosynthesis of nucleotides 246
in cobamide enzyme formation 250
in enzyme function 246
of bile salts in digestion of fats 119
of free radicals in biologic systems 276
of vitamin 316
of xenobiotics in disease 274
ROS 276, 277
biological system 276
mitochondrial 277

S

Salvage pathway 157, 159, 166
of pyrimidine 166
Sarcomere 285, 301, 302, 303, 304
Skin 58, 59, 83, 141, 198, 226, 229, 247, 249, 264, 292, 293, 329, 330, 331, 341, 347, 348, 349
biopsy 264
cancer 198
erosion 247
fragile 330
infection 83
pigmentation 331
Sleep apnoea 339
Sleepiness constipation sensitivity 352
Sphingolipids 16, 18, 87, 99
Sphingomyelin 17, 18, 87, 91, 155
Sphingophospholipids 88
Sphingosines 17, 18, 88, 89, 91, 92
Splitting stage reaction 69
Squamous metaplasia of epithelial surface cells 226
Steroid hormone synthesis detoxification 4
Sub-cellular fractionation (SCF) 12
Succinate 42, 80

analogue inhibitor 42
thiokinase 80
Succinyl CoA 78, 79, 80, 98, 99, 106, 140
synthase 79
Sucrase deficiency 66
Sulfur conjugation of drugs 154
Superoxide dismutase (SOD) 45, 244, 279, 280
Syndrome 112, 143, 145, 225
carcinoid 143, 145, 225, 244, 266, 335, 353
chylomicron 112
korasakoff 225
malabsorption Kearns-Sayre 266
nephrotic 244, 335
pituitary thyroid hormone resistance 353
Synthase 43, 50, 52, 105, 138, 143, 163, 164, 165
aminoadipic semialdehyde 143
cystathionine 138
enzyme UMP 163
fatty acyl 105
thymidylate 50, 165
Synthesis 5, 7, 12, 32, 73, 76, 115, 131, 134, 145, 147, 148, 149, 154, 163, 164, 166, 171, 173, 175, 244, 246, 248, 346, 354
catecholamine 145
creatine 145
glycoprotein 154
of aldosterone 346
of eicosanoids 115
phospholipid 32, 244
porphyrin 248
pyrimidine 12, 163, 164
rhodopsin 246
thyroid hormone 354

T

Telomerase reverse transcriptase activity 177
Thermogenesis 341
Thermophilic bacteria 47
Thiophorase 102, 107, 108
Thrombocytopenia 262, 289
Thrombosis 137
Thrombosthenin 288
Thyroid 262, 351, 352
function tests (TFTs) 262, 351
hormone biosynthesis 351
stimulating IgG (TSI) 352
Thyrotoxicosis 352
autoimmune 352
Tobacco smoke components 272
Topoisomerases 172, 212, 213
Toxic 264, 267, 273, 299, 318, 321, 352
metabolic wastes 321
metabolites 264, 267, 273, 318
multinodular goiter solitary 352
shock syndrome toxin 299
Transaminases 46, 73, 80, 141, 226
Transcription process 184
Transferase 38, 42, 46, 104, 105, 138, 165, 193, 248, 269
adenine nucleotide 42
carnitine acyl 104
carnitine palmitoyl 105
glucuronsyl 269
glycosyl 248
peptidyl 193
phosphoribosyl 165
Translation process 179
Translocase enzyme 105
Translocases 46
Trans-octadecenoic acid 89
Transport 1, 15, 26, 28, 42, 151, 228, 309
defect 26
disorders 151
membrane proteins 309
mechanisms 1
of solutes 15
protein 28, 42
substances 228
Trauma 247, 278
Treatment of deficiency of urea cycle 133
Treatment of thyrotoxicosis 352
Triose phosphate 46, 49
dehydrogenase 49
isomerase 46
Tryptophan 26, 136, 200, 244
deficiency 26
degradation products 136
operon 200
pyrrolase uricase 244
Tubular function test 336
Tumor(s) 71, 204, 206, 207, 208, 209, 210, 323, 338, 339, 348
cells Defects 71
familial retina 206
necrosis factor (TNF) 208, 209, 210
non-pituitary 348
suppressor genes tumor 206

Tumor suppressor genes 204, 206, 208, 213
and oncogenes 204, 213
Turner syndrome 329, 334
Tyrosinase 45, 244
Tyrosine 26, 121, 140, 141, 142, 143, 244
hydroxylase 143
metabolism 140
Tyrosinemia 133, 141, 255

U

Ulceration 83, 225
corneal 225
Urea 14, 24, 165, 285, 287, 312, 313, 321, 324, 325, 326, 327, 336
and pyrimidine synthesizing pathway 165
clearance 326, 336
renal function 325
Urea cycle 131, 133, 134, 135, 136, 146, 165, 258, 265
defects 165
disorders 135, 258, 265
enzymes 133, 165
hyperammonemia 136
Uric acid oxidase 14
Uridine kinase 166
Uridyl transferase 73
Urinary 136, 137, 229
excretion, increased 137
oxalates 136
salt loss 229
Urine 83, 136, 137, 138, 141, 142, 143, 144, 228, 229, 234, 252, 261, 262, 323 325 326, 336
acidification 325
bilirubin 323
copious 83
maple syrup 144
Urolithiasis 162
Uronic acid 60, 75
pathway 75
Uterine hemorrhage 241

V

Vaccines 285, 299, 300, 301
adjuvant 300
killed 301
live 301
Valinomycin 27
Vesicles 4, 8, 9, 26, 308, 310
forming endocytic 26
intracellular 9
secretary 4
synaptic 308
Viral infection 209
Virus 300, 301
active 301
attenuated 300
inactivated 301
Vitamin 88, 143, 156, 222, 223, 224, 225, 226, 227, 228, 238, 239, 240, 246, 250, 251, 282, 283, 316
B12 250
dietary 156
niacin 143
soluble 88
synthesize 283

W

Water 223, 224, 225, 229, 282, 285
intoxication 282
losses, urinary 229
salt balance acid-base 285
soluble vitamins 223, 224, 225
Whipple's disease 95
Wilson's disease 245, 282, 322

X

Xanthine 45, 46, 153, 161, 253, 277
alcohol dehydrogenase 46
oxidase 45, 161, 253, 277
Xanthurenicaciduria 144
Xeroderma pigmentosum (XP) 178, 198, 334
Xerophthalmia 226

Y

Yield stage reaction 69

Z

Z-disks 302, 304
of sarcomeres 302
Zellweger syndrome 97

Zinc 201, 246, 247
deficiency 246, 247

SIMMI KHARB

Dr. Simmi Kharb completed her MBBS in 1989 and MD (Biochemistry) in 1995 from Pt. B. D. Sharma PGIMS, Rohtak, India. She has an extensive teaching and research experience in the field of Medical Biochemistry, Medical Biotechnology, and Clinical Chemistry, and has published 224 papers in Indexed Journals (152 International, 72 National) in the area of pathophysiology of pre-eclampsia, free radicals, diabetes, leukemia, cancer and myocardial infarction (MI). Her research on free radical biology, antioxidants, nutraceuticals, and Vitamin E & C supplementation in diabetes, MI, neonatal jaundice, leukemia and pre-eclampsia has been published in more than 30 international papers and cited in more than 300 papers. She has also worked in the area of congenital toxicology and origin of diseases, and her research on fluoride toxicity has been appreciated at several national and international scientific platforms.

Besides being a Senior Professor and Head in the Department of Biochemistry at Pt. B. D. Sharma PGIMS, Rohtak since 2008, she is also holding the positions of Nodal Officer for DHR-Multidisciplinary Research Unit, State Nodal Officer for AB-PMJAY Costing of Health Services in India project and Regional coordinator for Dr. Padam Singh Research and Development Scheme at the institute, and Member Secretary for Ph.D. & NAAC Assessor at Pt. B. D. Sharma UHS, Rohtak, since 2019.

She is trained in human whole genome sequencing and holds experience in supervising quality control systems in clinical chemistry labs, and is trained in microarray technology, proteomics nanotechnology, immobilized enzymes for sensors, cord blood banking, stem cell therapy, and molecular forensics. Her profile is mentioned in the "Marquis Who's Who in World" and "Marquis Who's Who in Science and Engineering". She has handled many research projects and received research grants from both central and state government bodies. She has also refereed the project for MDRS Mission (Mars Desert Research Station), NASA, USA.