University of Tripoli
Faculty of Medicine
Department of Biochemistry and Molecular Biology
Curriculum of Biochemistry and Molecular Biology

A) Teaching in Biochemistry Department started in the academic year 1974 – 75. The department conducts teaching of Biochemistry to the first 4 semesters (each semester consist of 14 weeks + 2 weeks exams).

B)

Course	Lectures (weekly)	Practical (weekly)	Tutorial (weekly)
BC120	**2 hours**		**1 hour**
BC141	**3 hours**	**2 hours**	**1 hour**
BC142	**3 hours**	**2 hours**	**1 hour**
BC243	**3 hours**	**2 hours**	**1 hour**

1st Semester (BC120)
28hours

I- INTRODUCTION (10 Lectures)
Biomolecules, Chemical bonds, Organic chemistry, Functional groups, Aliphatic and aromatic hydrocarbones.

II- WATER AND ACID – BASE EQUILIBRIA (4 Lectures)
-Water as a solvent, water is nucleophilic, interaction of biomolecules with water, forces stabilizing biomolecules, polar and non-polar, hydrophobic and hydrophilic molecules.
- Dissociation of water: ion product of water
- Acid – Base equilibrium: dissociation of a weak acids, pH and pKa, titration of weak acids, Henderson-Hasselbach equation.
- Buffers: Regulation of blood pH, physiological buffers,
- Role of liver, Kidney and lung in regulation of blood pH, imbalances of blood pH (alkalosis and acidosis).

III- CHEMISTRY OF AMINO ACIDS AND PROTEINS (6 Lectures)
- Function of proteins
- Amino acids: Structure, optical activity, amphoteric properties, chemical, nutritional and metabolic classification of amino acids.
- Peptides and polypeptides: formation of peptide bond and polypeptide chain, conformation of proteins (primary, secondary tertiary and quaternary structures), separation methods of proteins.
- Digestion and absorption of proteins and clinical correlations.

IV- CHEMISTRY OF CARBOHYDRATES OF PHYSIOLOGIC IMPORTANCE (4 Lectures)
- Biomedical importance

- Carbohydrate functions, nomenclature, classification and structures, glycosidic linkages, cyclization and isomerization of monosaccharides, derivatives of monosaccharides (sugar phosphate, deoxysugars, sugar alcohol, sugar acid and ascorbic acid.)
- Reducing and non reducing disaccharides.
- Polysaccharides: homopolysaccharides and heteropolysaccharides.
- Glycoconjugate: Proteoglycans, Glycoproteins and Peptidoglycans.
- Digestion and absorption of carbohydrates and clinical correlations.

V- NUCLEOTIDES AND NUCLEIC ACIDS (4 Lectures)
- Structures and functions of purines and pyrimidines, nucleosides and nucleotides, nucleotides derivatives, nucleotide triphosphate and group transfer potentials, polynucleotides.
-Nucleic acids are polymer of nucleotides, DNA and RNA structure, function, types and properties.

2nd Semester (BC141)
42 hours

VI- CHEMISTRY OF LIPIDS OF PHYSIOLOGIC IMPORTANCE (4 Lectures)
- Biomedical importance.
- Lipids definition, functions, structures and classification (simple, complex and derived lipids)
- Fatty acids: nomenclature, general properties and classification (chemical and nutritional).
- Triacyglycerols, phospholipids and glycolipids
- Steroids: definition, structure and function
- Lipid peroxidation.
- Separation and identification of lipids.
- Digestion and absorbance of lipids and clinical correlation

VII- VITAMINS AND COENZYMES (12 lectures)
- Definition, structures, active forms, functions and classification, sources, transport, requirements, deficiency and toxicity of water - soluble and fat – soluble vitamins.
- Coenzymes classification, metabolic and vitamin derived coenzymes, e.g ubiquinone (coenz - Q), protein coenzymes (cytochromes and thioredoxin).

VIII- ENZYMES (12 Lectures)
- Biomedical importance
-General concept: definition, nomenclatures, general properties, structure, distribution, proenzymes, enzyme classification according to structure and reaction they catalyze, enzyme cofactors.
- Enzyme activity: enzyme unit, specific activity, turnover number, enzyme assay, enzyme specificity, active sit.
- Enzyme catalysis: proximity, strain, covalent and acid – base catalysis
- Factors affecting enzyme activity, Michaelis- Menten equation, Km significance, Lineweaver-Burk plot of enzyme activity.

- Enzyme inhibition: irreversible inhibitors, general and specific inhibitors, reversible enzyme inhibition (competitive, non comp. and uncomp.), clinical applications of enzyme inhibition.
- Regulation of enzyme activity (allosteric, reversible covalent modification and regulation by control proteins (calmodulin)
- Isozymes: examples, separation and clinical application

X- BIOENERGITICS (6 Lectures)

- Free energy, endorganic reactions (anabolism), exorganic endorganic reactions, other high energy compound, sources of ATP.
-Biological oxidation, free energy and oxidation reduction potential (redox potential)
-The electron transport chain (E.T.C), location, components, energy span and redox span of E.T C, inhibitions of E.T.C.
-oxidative phosphorylation, chemiosmotic theory, inhibition of oxidative phosphorylation, uncouplers (chemical and natural)
-Aerobic oxidation of cytosolic NADH, Glycerol phosphate and malate aspartate shuttle.
- Transfer of energy from mitochondria; the creatine shuttle.

XI- BODY FLUIDS AND NUTRITION (8 Lectures)

-Body fluids (intracellular and extracellular), composition in health and disease.
Nutrition: Dietary reference intake, energy requirements in human, energy content of food, resting metabolic rate, thermic effect of food, physical activity.
- Dietary fats: dietary fat and plasma lipids, relation with coronary heart disease.
- Dietary carbohydrates: requirements, dietary carbohydrates and blood glucose.
- Dietary proteins: quality of proteins, nitrogen balance, requirements of proteins, protein caloric malnutrition (Kwashiorker and Marsmus).
- Mineral and trace elements: body minerals, functions, ranges, toxicity and deficiency symptoms

3rd Semester (BC142)
42 hours

Carbohydrate metabolism (10 Lectures)

I Digestion and absorption of carbohydrates, transport of glucose and rate of absorbed sugars.
- Insulin, receptors and glucose transporters.
-Glycolysis (aerobic and anaerobic), free energy.
II Changes of glycolysis, alternative fate of pyruvate, regulation of glycolysis.
- Clinical aspects impairment of pyruvate metabolism and lactic acidosis, pyruvate kinase deficiency.
III The citric acid cycle: entry of pyruvate to mitochondrion, conversion of pyruvate to actetyl CoA (PDH complex)
PDH complex regulation, oxidationof actyl-CoA, free energy changes of citric acid cycles and its relation to E.T.C, regulation of citric acid cycle, pivotal role of citric acid cycle in metabolism

IV Glycogen metabolism: synthesis and degradation of glycogen in liver and muscles, hormonal regulation of glycogen phosphorylase and synthase, glycogen storage diseases.
V Gluconeogenesis: reaction and regulation of gluconeogenesis (hormonal, substrate availability and allosteric)
VI The pentose phosphate pathway and other pathways for hexoses:
reactions of the pathway, uses of NADPH, role of glucose-6-p dehydrogenase and its deficiency, regulation of pentose phosphate pathway, the reciprocal regulation of glycolysis and gluconeogenesis.
- Uronic acid pathway.
- Metabolism of fructose and galactose
- Clinical aspects, erythrocytes hemolysis in pentose phos. Pathway impairment, defects in fructose metabolism (essential fructosuria, hereditary fructose intolerance, fructose (sorbital and diabetic cataract), enzyme defects in galactose metabolism (galactosemia).
VII regulation of blood glucose: Metabolic and hormonal regulation, hyperglycaemia, diabetes mellitus (types, symptoms and treatment) hypoglycaemia, the renal threshold of glucose, glucose tolerance test.

Lipid metabolism (12 Lectures)
- I Digestion, absorption and fate of dietary lipids, defects in lipid digestion (steaterrhae and chylurea).
- II Fatty acid synthesis and ecosonoids:
Sources of actyle –coA and its transport to the cytosol, sources, sources of NADPH, formation of malonyl-co A, fatty acid synthesis complex reaction.
-microsomal and mitochondrial systems of fatty acid elongation, synthesis of unsaturated fatty acid.
- Regulation of fatty acid synthesis, storage of fatty acid as components of TAG (fate of TAG in liver and adipose tissues).
- Essential fatty acids deficiency.
- Eicosonoids synthesis and physiological actions.
III – Fatty acid oxidation and keton bodies.
- Mobiliation of stored fats; release of fatty acids, hormone sensitive lipase, fate of glycerol and fatty acid.
- Fatty acid oxidation, fatty acid transport into mitochondria.
- β – oxidationof fatty acids, β – oxidation of unsaturated and odd chain fatty acids, energy yield from fatty acids oxidation, peroxisomal oxidation of fatty acids.
- Regulation of fatty acid oxidation.
- Disorders of impaired fatty acid oxidation: Zellweget disease, Refsum disease, Carnitine and Palmitoyl transferase deficiency, dicarboxilic aciduria.
- Keton bodies formation: Synthesis of keton bodies (ketogenesis), utilization of keton bodies (ketolysis).
- Regulation of ketogenesis, importance of ketone bodies and energy yield from their oxidation, exclusive ketogenesis (ketosis) and diabetes mellitus (metablic change, symptoms and management).
- IV Complex lipids metabolism

-Phospholipid synthesis (phosphatidyl ethanolamine, phosphotidyl choline, phosphotidyl serine, phosphotidylinositol synthesis.
-phosphotidylglycerol, cardiolipin, sphingomylin sphingomylin degradation.
-Glycolipids, disorder of phospholipids metabolism, demyelination disease (multiple sclerosis) respiratory distress syndrome, lipid storage disease (sphingolipidosis)
V- Lipid transport (lipoprotein metabolism)
- Plasma lipoprotein; classification, site of formation and function, apolipoproteins, structure and function, lipoprotein lipase, tissue distribution, activation and deficiency.
VI Cholesterol metabolism
- Cholesterol function biosynthesis and its regulation
- Plasma lipoproteins and transport of cholesterol, function of bile acids, enterohepatic circulation of bile, function of bile acids, cholelthiasis.
- Plasma cholesterol normal range, hyper- and hypo- cholesterolemia.
-Serum cholesterol and atherostorosis and coronary heart disease, life style, diet and cholesterol levels, hypolipidemic drugs
- Fatty liver (causes and management), liptropic factors.
- List factors for atherosclerosis and heart disease.

Protein and amino acids metabolism (10 Lectures)
- Protein turnover, digestion and transport of dietary proteins.
- Transport of amino acids, γ – glutemyl cycle for amino acid transport.
- Biosynthesis of nutritionally non-essential amino acids.
- Catabolism of proteins and of amino acid nitrogen, protein turnover, biosynthesis of urea, reactions of urea cycle, regulation of urea cycle and metabolic disorders of urea cycle.
- Ammonia formation, transport and toxicity.
- Nitrogen balance.
- Catabolism of the carbon skeletons of amino acid.
- Transamination, oxidative deamination, transmethylation, decaroboxylation reaction of amino acid.
- Conversion of glucogenic amino acids into pyruvate
- Conversion of ketogenic amino acids into acetyl – CoA.
- Metabolic disorders associated with glycine metabolism.
- Conversion of amino acids to specialized bioproducts.
- Inborn error of amino acid metabolism (PKU), albinism.
- Alkaptonuria, cyctinuria (homocystinuria) hartnap disease, maple syrup urine disease

Metabolism of Purines and Pyrimidines (5 Lectures)
I- Digestion and absorption of dietary nucleoproteins and nucleic acids Synthesis of 5-phosphoribosyl-1-pyrophosphates (PRPP).
- Biosynthesis of purine nucleotides and its regulation, salvage pathway for purine nucleotides, reduction of ribonucleoside diphosphate to deoxyribonucleotide diphosphate.
- Degradation of purine nucleotides.

- Biosynthesis of pyrimidine nucleotides and its regulation, salvage pathway for pyrimidine.
- Degradation of pyrimidine nucleotides.
- Inhibitors of purine and pyrimidine metabolism and their clinical applications.
- Diseases associated with defects of purine and pyrimidine metabolism; Gout, lesch-Nyhan syndrome, Von Gierk's disease, orotic aciduria and immunodeficiency disorder (adenosine deaminase deficiency and purine nucleoside phosphorylase deficiency).

Integration of Metabolism (5 Lectures)
- Metabolism; catabolism and anabolism, stages of metabolism; digestion and absorption, building of biomolecule in cytoplasm (anabolism) and catabolic stage in mitochondria.
- Metabolic fuels, fed, fasting, refed and starvation states.
- Strategy of metabolism; ATP, reducing power and building blocks.
- Metabolic regulation: non hormonal and hormonal regulation.
- Major metabolic pathways regulation and control sites (glycolysis, citric acid cycle, gluconeogensis, pentose phosphate pathway, glycogen synthesis and degradation, fatty acid synthesis and breakdown.
- Hormonal regulation of metabolic pathways; insulin, glucagons and epinephrine.
- Metabolic key junctions; pyruvate, acetyl-CoA and glucose-G-phosphate.
- Metabolism of specialized tissues: liver, heat, brain, skeletal muscles, adipose tissues, kidney.
- Diabetes mellitus.

4th Semester BC243
42 hours

Expression of Genetic information (12 Lectures)
- DNA replication and repair.
- Transcription and RNA processing.
- Protein synthesis.
- Mutations.

I *-Introduction: DNA structure and organization.*
II - *DNA replication and repair:*
- DNA replication in prokaryotes requirements, DNA polymerases, steps of replication (initiation, elongation and termination).
- DNA replication in eukaryotes, requirements, eukaryotes DNA polymerase, steps of replication (initiation, elongation and termination)
- Drugs that affect DNA replication; anti-metabolites, substrate analogues, inhibitors that interact with DNA.
- DNA repair: major DNA repair systems; excision and purinic repair, uracil removal and direct repair.

III- *Transcription and RNA processing:*
- Types of RNA, promoters (eukaryotic and prokaryotic)
- Transcription in Prokaroyotes: prokaryotic RNA polymerase, steps of transcription (initiation, elongation and termination).

- Transcription in Eukaroyotes: eukaryotic RNA polymerase, steps of transcription (initiation, elongation and termination, DNA elements that regulate initiation (enhancers and silencers).
- Inhibitors of transcription.
- Post transcriptional modification (RNA processing)
- Prokaryotic RNA processing.
- Eukaryotic RNA processing.
- ***IV*** *The genetic code and protein synthesis:*
- The genetic code; features of the genetic code, wobble hypothesis.
- Amino acid activation (amino acyl tRNA formation)
- Protein synthesis: initiation, control points in initiation, elongation and termination, polysomes, inhibitors of protein synthesis, post transcriptional modifications.
- Mutation: Base substitution, insertion and deletion of bases.

Regulation of gene expression and recombinant DNA (15 Lectures)
- ***I*** *biomedical importance*
- Importance of gene expression regulation for development, differentiation and adoption, types of responses of biological systems for a regulatory ligands.
- II *Regulation of gene expression in prokaryotes:*
- Operon as a model for regulation of gene expression. Lactose operon (an example of inducible operon) and tryptophane operon (an example of repressible operon) .
- III *Regulation of gene expression in Eukaryotes:*
- Alteration in gene content and position
- Transcriptional regulation: chromatin remodeling, enhancers and repressors elements, response elements (steroid hormones regulated genes, heat shock response gene), combination of DNA element with associated protein, motifs that regulate DNA binding to associated proteins.
- Eukaryotic genes amplification and rearrangement during development or in response to drugs.
- Control of gene expression in RNA processing (post transcriptional regulation)
- Translational regulation: rate of translation regulation (haem and β-globin translation), protein modification (proinsulin to insulin), protein degradation rate.
- **IV** *Recombinant DNA:*
- Definition, tools of recombinant DNA (restriction enzymes, DNA and RNA dependent polymerase, and DNA ligase).
- DNA cloning: Basic strategy of cloning, vectors (plasmid and bacteriphages), DNA libraries (genomic and complementary DNA libraries), cloned DNA fragments sequencing, probes, blotting (southern, Western and Northern).
- Restriction fragment length polymorphism (RFLP) - use of RFLP linkage analysis in identification of a mutant gene causing disease.
-DNA fingerprinting and its use.
- Application of gene cloning to produce recombinant protein, insulin and growth hormones as examples.
- Polymerase Chain Reaction (PCR): steps, advantages and application.
- Genetic disease; gene therapy, gene developing vectors, gene replacements therapy, gene delivering vectors, gene replacement therapy, transgenic mice, introducing a cloned gene into a fertilized ova or into embryonic stem cells.

-The gene – Cancer connection: protoncogenes, oncogenes, tumor suppressor genes (P53 gene).

Clinical enzymology (7 Lectures)
- Clinical application of enzymes: use of enzymes (and isozymes) in the diagnosis and prognosis of diseases, enzymes as reagents, enzymes as labeling reagents in enzyme-linked immunoassay (ELISA), enzymes as therapeutic agent.
- Plasma specific enzymes and their clinical significance.
- Non-plasma specific enzymes and their clinical significance.
- Pathological events leading to enzyme release in plasma (ischaemia, shock, toxic and inflammatory conditions, mechanical and physical destruction of cells, effects of the above factors on the cell metabolism and the cell membrane.
- Transport of intracellular enzyme release to extracellular environment (liver, heart, brain enzymes…etc)
- Examples of clinically important enzymes : , enzymes in cardiovascular disease of myocardial infarction, enzymes in gastroenterology, enzymes in hepatobiliary disease, enzymes in kidney diseases, enzyme tests in malignancies, enzyme assay to evaluate degree of toxicity and deficiency of some vitamins (or cofactors).

Porphyrin and Bile pigments (4 Lectures)
Chemistry: Types and occurrence of hemoproteins, structures, physical and chemical properties of hemoglobins, myoglobin.
Metabolism: Biosynthesis of porphyrin ring system, catabolism of hemoglobin and prophyrins, formation of bile pigments porphyria and prophrinuria.
Normal hemoglobins, adult, new born and embryonic. The organization of the human hemoglobin genes.
Abnormal Hb mutations e.g. Hbs, HbM etc. Thalasemia.

HORMONES (4 Lectures)
- ***I*** *Biomedical importance,* definition, classification by; site of synthesis, chemical structure and water solubility.
- ***II*** *hydrophilic hormones:*
- Cell surface receptors, transmembrane receptors, adrenergic receptors, insulin receptor, atrial natriuretic factor (ANF) receptor, guanylate cyclase, cGMP, nitric oxide and cGMP.
- Cell surface receptor and G-protein (signal transduction)
- Adenylate cyclase pathway; cAMP as a second messenger, cAMP-dependent protein kinases, phosphoprotein phosphatases, phosphodiesterases, hormone that act through adenylate cyclase pathway; insulin and epinephrine as examples.
- Phosphinositide pathway : phospholipase C (PLC) activation, generation of second messengers and cell activation, phorbol esters and protein kinase activation and cell proliferation (tumor promoters), Ca+2 as a second messenger.
- Abnormal G-protein and disease: ADP-ribosylation of Gsγ as in cholera toxin and pertussis toxin, cAMP and phophoinositide pathway.
- ***III*** *Lipophilic hormones:*
- Mechanism of action, intracellular receptors, hormone response elements (HRE), nuclear receptors, examples; steroid and thyroid hormones

- ***IV*** *Examples of endocrine hormones* (synthesis, structure, function ...etc*)*
- Pituitary hormones; e.g growth hormone.
-Hormones of Ca+2 metabolism; parathyroid hormones and calcitonin, Ca+2 haemostasis.
- Hormones of intracellular activation, eg. Thyroid hormones, glucocortcoide and mineral corticoids.
- Pancreatic hormones: insulin and glucagen.

Marks Distribution

BC120 Midterm 30% + Final exam 70%

BC141, BC142, BC243
Midterm exam 20% + Practical 20% + Final exam 60%

Pass mark is 60%

References:

1. Harper's Biochemistry by: Robert K. Murray.
2. Lippincott's illustrated reviews by: Denise R. Ferrier
3. Clinical Biochemistry by: Gaw et al