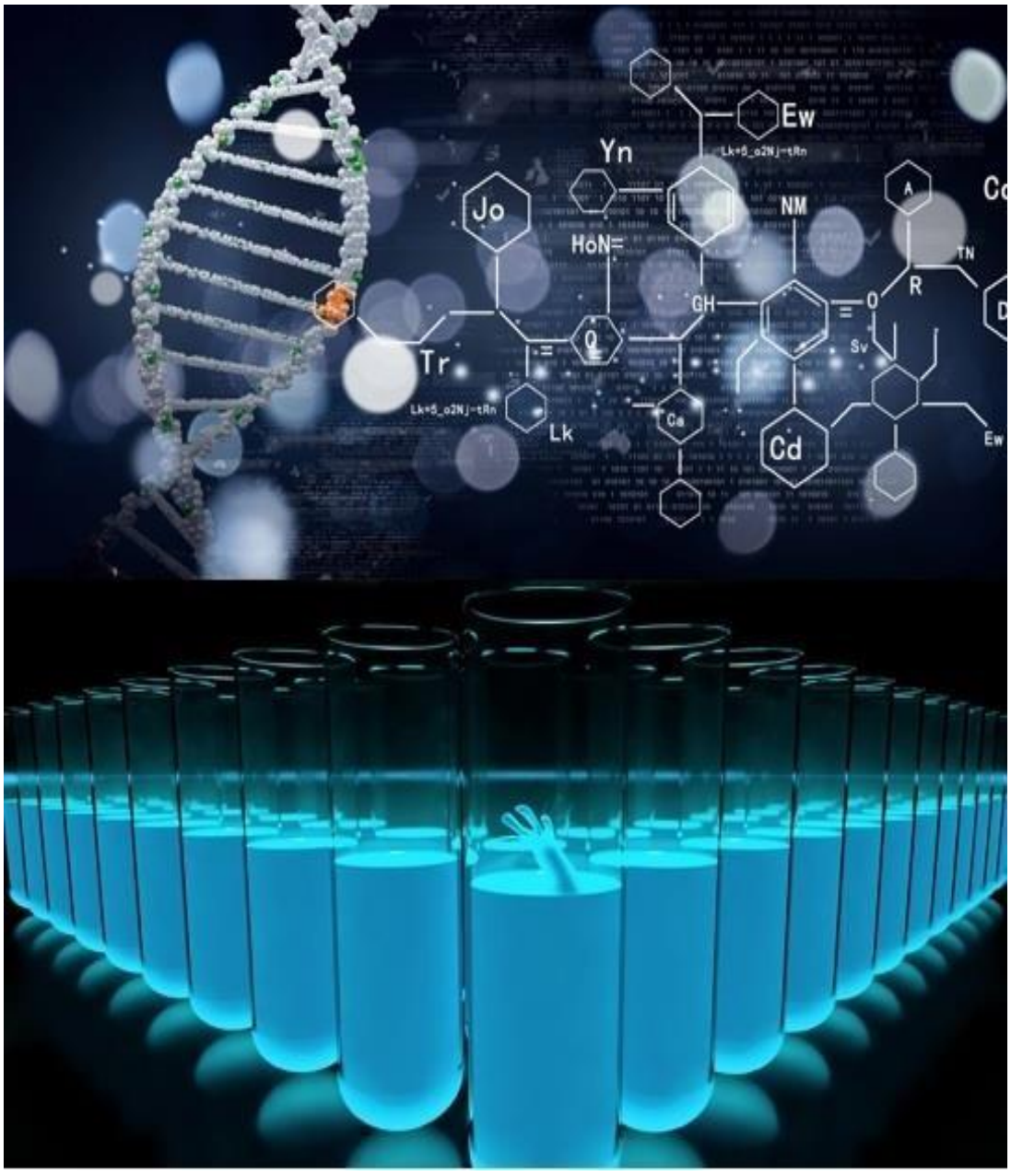
BIOCHEMISTRY
STUDENT HANDBOOK



BIOCHEMISTRY
STUDENT HANDBOOK

DEPARTMENT OF BIOCHEMISTRY
FACULTY OF MEDICINE
SABARAGAMUVA UNIVERSITY OF SRI LANKA

TABLE OF CONTENT

MESSAGE FROM THE DEPARTMENT

Dear Students,

'Biochemistry' is the study of the chemical basis of life, in other words, it is the application of chemistry to the study of biological processes at the cellular, molecular and sub-molecular levels. Knowing the Biochemistry helps to understand the molecular basis of diseases, current therapies, and action of new drugs. In future, therapies will possibly involve gene rather than organ transplants. Pharmacogenomics and Nutritional genomics will create a basis for designer treatments customized to an individual's genetic makeup. To understand all this it is essential to know functional interactions between metabolic pathways, organs and tissues.

This is course is designed to cover the aspects of Biochemistry relevant to medicine. A good knowledge of Biochemistry enables a student to understand normal healthy life and disease at molecular level.

This handbook has been prepared to cover the information you will need for your programme and to assist you as a student. Please read it through and use it as a first point of reference.

We in the Department of Biochemistry while extending you a warm welcome to the youngest Medical School in Sri Lanka, wish you a happy and memorable stay with intellectual advancement and mental tranquility.

Yours

Staff/Department of Biochemistry.

STAFF MEMBERS OF THE DEPARTMENT

ACADEMIC STAFF MEMBERS

Professor Nirmali Wickramaratne	Ph.D. in Biochemistry (USA), Grad. I. Chem.C.
Dr. N.D. Amal Wageesha	Ph.D. in Biochemistry (Col), M.Phil in Biochemistry (USJP), Grad I Cham C, M.I.Chem C.
Dr. I.H.V. Nicholas	Ph.D. in Biochemistry (UOP), BSc. (Chemistry Sp.) (USJP)
Dr. Sumeth Perera	Ph.D. (Oxon), MPhil, MRes DIC, BD, BSc (Hons)
K. Nadeesha Nilmini	BSc.(Nutrition)

RECOMMENDED READING MATERIAL

- Lippincott's Illustrated Reviews – Biochemistry, Harvey RA (ed), 8th edition, 2013, Lippincott Williams & Wilkins, Philadelphia.

- Harper's Illustrated Biochemistry, Murray R, Rodwell V, Bender D, Botham KM, Weil AP, Kennelly PJ30th/31stedition

- Textbook of Biochemistry with Clinical Correlations, Devlin TM, 7th edition, 2010, John Wiley & Sons, New York

- Lehninger principles of biochemistry (6th Edition) Nelson, D., and Cox, M.

- Biochemistry. Jeremy M. Berg, John L. Tymoczko, Lubert Stryer 7th Edition

- Molecular Biology of the Cell (Sixth Edition) by Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, Peter Walter.

- Nutritional Biochemistry 2nd Edition by Tom Brody.

- Nutritional Biochemistry and Metabolism: With Clinical Applications by Maria C. Linder.

OBJECTIVES

The teaching programmes of the Department of Biochemistry embody a fundamental approach to the chemistry of life and convey the strongly unifying contribution of biochemistry and molecular biology to other scientific disciplines. In order to understand a disease state, it is first necessary to study the normal pathways of the metabolism that is, the bio synthesis and break down of molecules, how different classes of biological molecules interact together to capture energy, build complex molecular machines, utilization of energy and regulation of metabolic pathways.

In addition you will be introduced to Clinical Biochemistry and to Molecular Biology to understand the disease processes at molecular level and modern methods of disease diagnosis.

By the end of the course, students should be able to:

1. Demonstrate knowledge and understanding of the molecular machinery of living cells.
2. Demonstrate knowledge and understanding of the principles that govern the structures of macromolecules and their participation in molecular recognition.
3. Describe the principles underlying enzyme catalysis.
4. Describe the mechanism of action of hormones and how they regulate biochemical pathways.
5. Explain how the genetic information is stored and transferred from generation to generation.
6. Explain how energy is generated, utilized and stored by various organs of the body.
7. Learn how metabolic pathways are regulated and how alteration of one pathway will affect the other.
8. Recognize how the abnormalities in biochemical processes lead to disease/s and the use of biochemical indicators in disease diagnosis.
9. Describe the requirement of micro and macronutrients by humans and how improper intake leads to various clinical conditions.
10. Discuss the importance of molecular biology in medicine.

Your knowledge acquired in this course will enable you to integrate Biochemistry with other basic and clinical sciences and should be able to apply biochemical principles to understand the pathophysiology of disease.

TEACHING/LEARNING METHODS

The teaching and learning methods includes lecture, practical sessions, guided learning sessions, small group discussions and tutorials.

While lectures provide you with basic information, small group discussions and tutorials give you an opportunity to discuss specific problems with your fellow students, and facilitators.

The laboratory practical and demonstrations will provide you the fundamental mechanism of disease diagnosis where some of these tests have to be carried out in a ward setting when you become a medical officer.

DETAIL EVALUATIONS

Assessments in the Department of Biochemistry

Biochemistry Semester-1
End of Semester assessment through a theory paper (End Semester Examination I)

Biochemistry Semester II
End of Semester assessment through a theory paper (End Semester Examination II)

Biochemistry Semester III
Final examination- (Bar examination/2nd MBBS examination)

EXAMINATION STRUCTURE AND FORMAT

a. End Semester Examination

These would be held at the **end of Semesters I, II and III** and will examine the knowledge acquired within that particular semester. This is a summative assessment.

End Semester Examination /Continuous Assessment (CA)			
Method of Assessment	Number of Questions	Marks allocated	Time allocated
CA 1			
MCQ	15 T/F	100%	45 min
SEQ	2	100%	40 min
Weightage		5%	
CA 2			
MCQ	15 T/F	100%	45 min
SEQ	2	100%	40 min
Weightage		7.5%	
CA 3			
MCQ	15 T/F	100%	45 min
Weightage		7.5%	
Final Examination /Third MBBS Part 11 Examination (Main)			
MCQ	40 T/F	30%	2 hr
SEQ	5	30%	1 hr 40 min
OSPE	20	10%	1 hr
OSVE		10%	10 min
CA 1, 2 & 3		20%	
Total marks		100%	
Final Examination / Third MBBS Part 11 Examination (Repeat)			
MCQ	40 T/F	30%	2 hr
SEQ	5	30%	1 hr 40 min
OSPE	20	10%	1 hr
OSVE		10%	10 min
Total marks		80% [upgrade to 100]	

MCQ – Multiple Choice Question
SEQ – Structured Essay Question
OSPE – Objective Structured Practical Examination
OSVE – Objective Structured Viva voce Examination
T/F – True & Fales type

***The End Semester Examinations will not be repeated**

b. The Final Examination in Biochemistry

There would be **three components** in the final assessment (Bar examination /2nd MBBS examination).

1. **A four (4) hour and 30 minutes theory paper covering the entire biochemistry syllabus.**

   The paper will contain **Forty (40) MCQs** (to be answered in 120 minutes) and **five (05) SEQ** (to be answered in 150 minutes).

2. **Objective Structured Practical Examination (OSPE).**

   This would be based on the practical classes, guided learning sessions and small group discussions conducted throughout the entire Biochemistry course (three semesters). The examination will be of one (1) hour duration and will consist of twenty (20) spot tests where the student will have to observe demonstrations laid out and answer the question / s based on each of them.

3. ***Viva Voce* Examination.**

Calculation of Final Mark for Biochemistry Final Examination (Bar examination /2nd MBBS examination).

Compilation of the final mark will be as follows;

Semester Examination I	**5**
Semester Examination II	**7.5**
Semester Examination III	**7.5**
Final Examination (Written)	**60**
OSPE	**10**
Viva Voce Examination	**10**
Total	**100**

4. Other conditions

1. No student can omit semester 1,2 and 3 (End Semester Examination I, II & III) examinations under any circumstances. In case of a valid Medical Certificate with University Medical Officers approval / Medical Board approval, 20% from the participated End semester examinations will be taken for calculation of the final marks for Biochemistry.

2. In the final Examination students should complete all components of the examination within one attempt (in one sitting). If a student failed to do so the student has to repeat the entire examination (final examination).

3. If a student is unable to attend the total/part of the final examination due to a valid medical reason the student should submit a recognized medical certificate. In such a case the student shall sit the full repeat examination. This attempt will be considered his/her **1st attempt**.

4. In order to '**Pass**' the student should have obtained a minimum of 50% in the Final Examination and a minimum of **45% in theory components** (the average of End Semester Examination I, II and III and the theory component of the Final Examination (MCQ and SEQ)).

5. Repeat Examination procedure (Final examination in Biochemistry)

The first repeat attempt for the failures will be conducted after a period of 4 weeks.
The second repeat attempt will be with the immediate junior batch.

If a student fails Final examinations (proper and repeat), he/she is given two more attempts with the immediate junior batch as 3rd and the 4th attempt.

If a student fails in all 4 attempts he/she will be deregistered.

6. Marks allocation for Repeaters (Final Examination in Biochemistry)

Final examination (Theory)	**70%**
OSPE	**20%**
Viva Voce	**10%**

*****'Semester Examination I, II & III are not considered'
Maximum grade that a repeat student can obtain is **50%** (Pass mark) only

ATTENDANCE

A student must achieve a **minimum of 80%** attendance for lectures, tutorials, practical and small group discussions (SGD). Failure to achieve the 80% attendance the student will not be allowed to sit the Final examination.

He/ She will be permitted to sit with the repeat examination and this attempt will be considered as a repeat attempt.

CRITERIA FOR DISTINCTION

The student will be awarded a 'Distinction in Biochemistry' if he/she obtained a minimum of 60% for End Semester Examinations (End Semester examination I, II and III) and a minimum of 70 % in the final examination, provided that the student has obtained these marks at his/her first sitting.

DETAILED LEARNING OUT COMES

Semester 1

Lecture topics

1. **Cell structure functions** 8 hours

The student should be able to

- Explain the general and the molecular structure of the cell membrane.
- Explain the importance of Proteins, Carbohydrates and Cholesterol in cell membrane.
- List major mechanisms of transport across membranes.
- Describe the principle of passive and active mediated transport.
- Explain the mechanisms of simple diffusion with example of voltage gated channels and ligand gated channels.
- Explain passive mediated (facilitated) transport with examples.
- Explain active transport using Na^+/K^+ATPase system in glucose, galactose and amino acids transport across the intestinal mucosal system and proximal tubule.
- Describe exo and endocytosis in macro-molecular transport with examples.
- Explain the biochemical importance of the composition of oral rehydration solution.
- Describe the action of ionophores.
- Identify inhibitors of active transport systems with applications in medicine.
- Explain the role of cytoskeleton in multi cellular organisms.
- List the chief cytoskeleton protein filaments and briefly describe their structure and functions.
- Explain tight junctions, desmosomes and gap junctions, indicating their functions.
- Identify the component of the extra cellular matrix and their basic functions.

Clinical correlations;

- List common disorders effecting the cytoskeleton.
- Explain the action of snake and similar animal venoms on the extracellular matrix.

2. pH and buffers 4 hours

The student should be able to

- Explain the structure and ionization of water
- Define pH.
- Explain how pH is determined.
- Explain the significance of buffering action, buffering capacity and buffering range.
- Explain Henderson-Hesselbalch equation and list its applications.
- Explain the iso-electric pH.
- List the important biological buffering systems in the human body.
- Should be able to list the most important buffering system/systems in blood, urine and cell.
- Describe the importance and mechanism of action of histidine in buffering action, Proteins/hemoglobin buffer system, Bicarbonate buffer system, Ammonia buffer system and phosphate buffer system.

Clinical correlations;

- Describe metabolic and respiratory acidosis and alkalosis.

3. Carbohydrates 4 hours

The student should be able to

- Describe the functions, chemical properties of carbohydrates.
- Describe structural differences of Aldoses and Ketoses.
- Recognize that monosaccharide units are linked together by glyosidic bonds to form disaccharides and polysaccharides.
- Identify the types of glyosidic linkages and their significance to humans.
- Describe reducing and non-reducing properties of sugars.
- Classify the polysaccharides and general structures of Glycogen, Starch and cellulose.
- Know the functions of sugar acids, alcohols and amines.
- Explain the basic features of glycosaminoglycans and recognize

that glycosaminoglycans link with proteins to form proteoglycans with examples.

- Compare glycoproteins and proteoglycans with respect to basic structure and functions.

Clinical correlations;

- Explain the biological functions of GAG in the joints.
- Explain the biological importance of glycoproteins as blood group substances.

4. Amino acids and proteins 6 hours

The student should be able to

- Classify and name the amino acids.
- Explain the acid-base properties of amino acids.
- Explain zwitterions and iso electric point(pI) of amino acids.
- Explain dehydration, decarboxylation and transamination reactions of amino acids.
- Describe the levels of organization of proteins and forces that stabilize these structures.
- Identify the sulfur containing amino acids.
- Explain the structure – function relationship of collagen, myoglobin and haemoglobin.
- Explain denaturation and identify the agents that do so and the non-covalent interactions that are affected with examples.
- Explain the methods of protein purification and separation and explain the underline principles of separation methods.

Clinical correlations;

- Explain the biochemical basis for the use of 70% alcohol as a disinfectant.

5. Lipids 4 hours

The student should be able to

- Explain the functions of lipids.
- Classify fats, waxes and oils.
- Describe the structure of saturated and unsaturated fatty acids, their nomenclature with examples.
- Describe essential fatty acids and their biological importance.
- Describe the structure of triacylglycerol and its general properties.
- Describe the structure of phospholipids and explain its amphipathic properties and biological importance.
- Describe the structure of sphingo-lipids, Glyco-lipids and their functions.
- Describe the structure of cholesterol and functions.

Clinical correlations;

- Explain how glycolipids responsible for blood clotting (blood clotting factors and their carbohydrate composition).

6. Nucleic acids 6 hours

The student should be able to

- Explain structures, functions and properties nucleic acids.
- Explain how and why DNA is packaged inside the eukaryotic cell.
- Explain semi conservative replication of DNA.
- Explain DNA repair mechanisms and the function and importance of telomerase.

Clinical correlations;

- Explain connection of telomerase to cellular aging and apoptosis.

7. Storage and Expression of Genetic information 6 hours

The student should be able to

- Explain the gene, genetic code gene expression and regulations.
- Explain the protein biosynthesis process.
- Explain post transcriptional and post translational modifications and their significance.
- Explain why amino acyl tRNA-synthetase consider as the 2nd genetic code.
- Describe what a mutation is and identify different types of mutations that can occur.
- Identify the implications of each type of mutations.
- Explain the role of chaperones in protein folding.

Clinical correlations;

- Explain how mutations can occur and understand the contribution of mutations to evolution.
- Give examples of diseases caused by protein misfolding.
- Explain the formation of prion proteins and implications.

8. Enzymes 6 hours

The student *should be able to*

- Explain the characteristic properties of enzyme.
- Explain how enzymes act (lock and key and induced fit models).
- Identify the six main classes of enzymes.
- Identify the factors that affect enzyme catalyzed reactions.
- Define Km and Vmax values using Michaelis- Menten and Line-Weaver and Burk plots.
- Recognize that the enzymes can be inhibited and explain different types of inhibitions using examples (competitive, non-competitive, uncompetitive and suicide inhibition).
- Illustrate graphically the different types of inhibitions.
- Explain the regulation of enzyme activities, *via* induction, repression, allosteric modulation and covalent modification.
- Classify cofactors.

Clinical correlations;

- Explain the use of enzymes in clinical diagnosis.
- Explain iso-enzymes and their use in clinical diagnosis.

9. Hormones 4 hours

The student should be able to

- Classify hormones based on their chemical structure and functions.
- Explain the need for hormone receptors.
- List the types of hormone receptors.
- Explain the operation of receptors for water soluble hormones.
- Explain the operation of receptors for lipid soluble hormones.
- Explain the role of G-proteins in hormone signal transduction.
- Explain up regulation and down regulation of hormone receptors.
- Explain the cascade effect of hormone signal transduction.
- Explain the role of second messengers in hormone signal transduction.

10. Bioenergetics and oxidative phosphorylation 4 hours

The student should be able to

- Explain the significance of malate and glycerol-phosphate shuttles.
- Recognize that reduced coenzymes serve as energy source for oxidative phosphorylation.
- Indicate the entry points of electrons from NADH and $FADH_2$ and explain the final reduction of O_2 to H_2O.
- Explain 'Mitchell's Chemiosmotic' hypothesis of ATP generation.
- Differentiate substrate level phosphorylation and oxidative phosphorylation.

  Clinical correlations;
- Explain the process of uncoupling of oxidative phosphorylation and its significance in brown adipose tissue.
- Explain the effect of inhibitors of the ETC.

Total Lecture Hours 52 Hours

Semester II

Lecture topics

1. **Digestion and Absorption of Carbohydrates and Introduction to metabolism** 4 hours

   The student should be able to

   - Understand Biochemistry of digestion & absorption of carbohydrates by salivary amylase, intestinal maltase, isomaltase, sucrase and lactase.
   - Identify the non-digestible carbohydrates and their role in digestion.
   - Explain the absorption of Glucose and Galactose from gut via SGLT and its operation.
   - Explain the role of different GLUT transporters and their distribution.
   - Explain the absorption of Fructose.
   - Explain the absorption of pentoses
   - Describe 'Anabolism' and 'Catabolism' and how ATP energizes energy requiring reactions

     Clinical correlations;
   - Explain the disorders of related to carbohydrate digestion and their biochemical significances (Lactase deficiencies, lactose intolerance and sucrase deficiency).
   - Explain the disorders related to carbohydrate absorption.

2. **Carbohydrate metabolism**

   a. Glycolysis and its regulation 2 hours

   The student should be able to

   - Explain how glucose is transported into cells.
   - Indicate the energy investing and energy harvesting phases of glycolysis.
   - Explain the regulatory steps of the glycolytic pathway *via* allosteric, covalent modifications and induction and repression.
   - Write the reactions where the reducing equivalences are generated.
   - Write the reactions where the ATP is synthesized.

- Explain the significances of substrate level phosphorylation.
- Explain the aerobic and anaerobic glycolysis and state the significance.
- Explain the difference of energy output under aerobic and anaerobic glycolysis.
- Explain the importance of glycolytic intermediates.

Clinical correlations;

- Explain glycolytic enzyme deficiency and their clinical significances.
- Explain why anaerobic glycolysis is predominant in malignant cells.

b.Metabolic pathways of lactose, **galactose and fructose** 2 hours

The student should be able to

a. Outline lactose, galactose and fructose catabolism.
b. Outline the synthesis of lactose in lactating mammary gland.
c. Explain the consequences of known deficiencies of enzymes in these pathways.
d. Explain the phosphate trapping due to excessive fructose consumption.

Clinical correlations;

e. Explain why fructose is not a substitute for sugar for uncontrolled diabetic.
f. Explain the biochemical basis of development of cataract in diabetics due to excess of glucose.
g. Explain why this is not happen in healthy individuals.

c. Acetyl CoA metabolism and TCA cycle 2 hours

The student should be able to

a. Indicate the reaction catalyzed by pyruvate dehydrogenase complex.
b. Explain why it is called pyruvate dehydrogenase complex.
c. List the coenzymes and vitamins required by pyruvate dehydrogenase.
d. Explain how the pyruvate dehydrogenase complex is regulated.

e. Indicate the formation of citrate from acetyl CoA.
f. Gives the sites and reactions of NADH, $FADH_2$, GTP and CO_2 formation in the TCA cycle.
g. Compare the oxidative decarboxylation of pyruvate and alpha- ketoglutarate.
h. Explain the regulation of TCA cycle.
i. Explain the amphibolic nature of TCA cycle.
j. Outline the anaplerotic reactions in TCA cycle.

d. Gluconeogenesis 2 hours

The student should be able to

a. Describe the five stages of glucose homeostasis in the fed and fasting states.
b. Indicate the entry points of gluconeogenic substrates to the pathway.
c. Describe the importance of gluconeogenesis.
d. Explain the role played by Insulin/Glucagon in regulation of gluconeogenesis.
e. Recall that the gluconeogenesis is a metabolically expensive pathway.

Clinical correlations;

f. Explain the stimulation of gluconeogenesis under stress.
g. Describe how excess ethanol consumption leads to fasting hypoglycemia.
h. Outline the importance of 'Cori cycle' and 'glucose – alanine cycle'.

e. Glycogen metabolism and regulation 2 hours

The student should be able to

a. Outline synthesis and breakdown of glycogen.
b. Describe the reciprocal control of glycogen metabolism.
c. Explain why muscle glycogen does not contribute to regulate blood glucose level.
d. Explain why muscle contraction triggers glycogenolysis.

Clinical correlations;

e. Explain the biochemical basis of glycogen storage diseases.

f. Hexose monophosphate pathway 2 hours

The student should be able to

a. State the significance of the oxidative and Non-oxidative phases of this pathway.
b. Explain why the oxidative pathway predominates in fat synthesizing tissues.
c. Explain why the non-oxidative pathway predominates in rapidly dividing cells.
d. Explain how the HMP pathway is linked to glycolysis.
Clinical correlations;
e. Describe the importance of HMP pathway in neutralizing strong oxidants.
f. Explain the heamolysis in glucose-6-phosphate dehydrogenase deficiency.

3. Lipid Metabolism and clinical correlations

a. Introduction to lipid metabolism 2 hours

The student should be able to

- Describe the emulsification of lipids with bile.
- Explain lipolysis of lipids by lipases.
- Explain the hydrolysis of cholesterol esters by pancreatic cholesterol esterase.
- Explain mixed micelle formation, mucosal uptake, resynthesize of tri-glycerides, chylomicron formation and secretion of them into the lymphatics.
- **Clinical correlations:**
  Explain the biochemical basis behind the disorders related to lipid digestion and absorption and their clinical significances (eg: Steatorrhea)

b. Fatty Acid biosynthesis and regulation 2 hours

The student should be able to

- Indicate that acetyl-coA is the precursor of fatty acid synthesis.
- Explain the role of citrate in fatty acid biosynthesis.
- Explain the role of acetyl CoA carboxylase in fatty acid biosynthesis.
- Expalin the regulatory role of acetyl coA carboxylase in fatty acid biosynthesis.
- Indicate the four types of reactions in fatty acid synthase complex.
- Indicate the role of NADPH in fatty acid synthesis.
- Indicate that 16 carbon palmitate is the end product of fatty acid synthesis.
- Explain the human de-saturases cannot incorporate double bonds beyond carbon 10 making lenoliec and linolenic acids essential.

Clinical correlations;

- Explain the biochemical basis of weight loss in individuals who are taking 'metformin'.

c. Beta oxidation of fatty acids and regulation 2 hours

The student should be able to

- Describe how the fatty acids are activated.
- Describe the transported of long chain fatty acids across the mitochondrial membrane.
- Describe the regulation of β oxidation.
- Explain the reciprocal regulation of fatty acid metabolism.
- State the biochemical importance of β oxidation.

d. Triglyceride & Phospholipid metabolism. 2 hours

The student should be able to

- Explain what a triglyceride is.
- Explain how TG can be made from glycerol-3-phosphate (from glycolytic DHAP and glycerol).
- Indicate why TG cannot be made from glycerol in the adipose tissue.
- Explain how TGs are hydrolyzed in adipose tissue.
- Explain the regulation of hormone sensitive TG lipase.
- Indicate that phospholipids are synthesized from DAG.
- Explain the amphipathic nature of the phospholipids.

Clinical correlations;

- Explain why TGs are hydrolyzed in starvation & uncontrolled DM.
- Explain the increase of FFAs in the blood in starvation & uncontrolled DM.
- Explain why FFA oxidation is increased in starvation & uncontrolled DM
- Explain the role of phospholipid lecithin as a lung surfactant.
- Explain the biochemical importance of lecithin in bile.

e. Ketone body synthesis and utilization 2 hours

The student should be able to

- List the ketone bodies.
- Explain when and why ketone bodies are produced.
- Explain the events that occur he renal tubules when KBs are filtered into the urine
- Explain why ketone bodies cannot be utilized by the liver.
- Explain how ketone bodies are utilized for energy.

Clinical correlation;

- Explain why KBs get filtered into the urine.
- Explain why glutaminase is activated in the kidneys in ketonemia.
- Explain why excessive production of ketone bodies leads to acidosis.
- Explain ketogenesis is activated in starvation & uncontrolled DM
- Explain a simple test you can use to identify ketone bodies in a sample of urine.

f. Cholesterol biosynthesis and bile acid metabolism 2 hours

The student should be able to

- Outline the biosynthesis of cholesterol and its regulation.
- Name the regulatory enzyme in cholesterol synthesis.
- Explain the effect of statins on cholesterol synthesis.
- Explain how the intracellular cholesterol level regulate its concentration within the cell.
- Outline the bile acid synthesis and its regulation and excretion.
- Outline the mechanism of cholelithiasis.

  Clinical correlations;
- Explain how the statins help to control hypocholesterolemia.
- Explain how the consumption of vegitables help to reduce serum cholesterol.

g. Eicosanoids and their metabolism 4 hours

The student should be able to

- List the eicosanoids.
- Outline the cyclo-oxygenase and linear pathways in the synthesis of thromboxane, prostaglandins and leukotrienes.
- Explain the two enzyme activities of prostaglandin synthase.
- Explain omega 3 and 6 fatty acids.
- Explain their significance in the synthesis of series 1, 2 and 3 eicosanoids.
- Explain the biological effects of series 1, 2 and 3 eicosanoids.
- Explain the effect of NSAIDs on the synthesis of eicosanoids.

  Clinical correlations;
- Explain the action of non-steroidal anti-inflammatory drugs (NSAIDS), aspirin and paracetamol on prostaglandin synthesis.
- Explain why the consumption of excess omega 6 FAs are not recommended.
- Outline the importance of balancing dietary omega 3 and 6 FAs.

3. Proteins and Amino acid Metabolism

i. Protein digestion, absorption and amino acid metabolism

6 hours

The student should be able to

- Identify the enzymes required for digestion of dietary proteins and explain their functions at different sections of the alimentary canal.
- Explain the absorption of proteins, peptides & di and tripeptides.
- Explain the 3 types of absorption of AAs from the intestinal lumen.
- Explain the role of transamination and deamination reactions in amino acid metabolism.
- Describe the central role of glutamate in amino acid metabolism.
- Identify the ketogenic and glucogenic amino acids.
- identify the specialized products synthesized from amino acids (Neurotransmitters, melanin, histamine).

Clinical correlations.

- Explain the development of food allergies.
- Identify acquired disorders of digestion & absorption.
- Identify inherited diseases of specific AA absorption (Hartnup Disease, Glycinuria, Cystinuria).
- Know the examples of in-born errors of amino acid metabolism (Phenylketonuria (PKU), albinism, Alkaptonuria (AKU) and maple syrup syndrome)

ii. Urea cycle and regulation of Urea Cycle

2 hours

The student should be able to

- Describe urea cycle and its regulation.
- Describe the exchange of amino acids among different organs.
- Describe the effects of enzyme deficiencies of the urea cycle.
- Describe why excess ammonia is toxic to the body.

Clinical Correlations;

4. Purine and pyrimidine metabolism 4 hours

The student should be able to

- Describe the *denovo* synthesis of purines and pyrimidines.
- Explain the regulation of *denovo* synthesis of purines.
- Describe the salvage pathway for purines.
- Explain the role of tetrahydrofolate (B_9) in purine and pyramidine biosynthesis.
- Explain the effect of enzyme deficiencies of the salvage pathway on the *denovo* syn thesis of purines.
- Explain purine catabolism and its end products.

Clinical correlations;

- Explain the biochemical causes of hyperuricaemia and the basis for the use of allopurinol in the treatment of gout.
- Describe the biochemical basis of anticancer drugs methotrexate and 5-fluorouracil.

5. Lipo-protein metabolism and clinical correlations 4 hours

The student should be able to

- List the types of lipoproteins.
- Describe different types of apo-lipoproteins and their functions.
- Outline the metabolism and functions of chylomicron, very low-density lipoproteins (VLDL), and high-density lipoproteins (HDL).
- Explain the mechanism of LDL uptake into tissues.
- Describe Frederickson-WHO classification of abnormalities of lipo-proteins.

Clinical Correlations.

- Explain why a fasting period is required before a lipid profile test.
- Explain why TGs are high in uncontrolled DM.
- Explain why a high blood LDL level is considered "unfavorable".
- Explain why a high blood HDL level is considered "favorable".
- Identify the electrophoresis of lipo-proteins and interpretation of lipid profiles.

6. Biochemistry of arthrosclerosis, cardiac markers and clinical correlations 2 hours

The student should be able to

- Describe the biochemical basis of atherosclerosis.
- Outline the risk factors for atherosclerosis.
- Explain the uses of cardiac markers in the diagnosis of myocardial infarction.
- explain the role of lipo-protein a (Lp a) in development of cardio vascular diseases
- Interpret laboratory reports.

Clinical Correlations.

- Explain why cigarette smoking facilitate atherosclerosis.
- Explain why it is desirable to maintain a good lipid profile.
- Explain the relationship between homocysteine and atherosclerosis.

7. RBC and Hemoglobin metabolism 6 hours

The student should be able to

- Describe the structure and distribution of heme in the body.
- Describe the heme metabolism.
- Describe the transport, hepatic uptake, conjugation and excretion of bilirubin.
- Describe different types of jaundice (hemolytic, intra and extra-hepatic cholestasis).

Clinical Correlations.

- Explain why a yellow colouration is seen in tissues in hyperbilirubinemia.
- Explain the pale colour stool in extra hepatic cholestasis.
- Explain the reason for the tea coloured urine in hepatitis.
- Explain the biochemical reason for Physiological jaundice.
- Interpretation of bilirubin profile and identify clinical correlations.

8. **Reactive oxygen and nitrogen species (RONS), their clinical applications and anti-oxidants.** 2 hours

The student should be able to

- Explain what is meant by RONS.
- Name the RONS generated within the body.
- Give the effects of RONS to the body and their clinical significances.
- Importance of neutralizing RONS and role of anti-oxidants.

Clinical Correlations.

- Explain the basis for the use of Vitamin C as an antioxidant.
- Explain the use of Vitamin. E as an antioixidant.
- Explain the protective role of NADPH and Glutathione.
- Explain the role of RONS against bacteria.

9. **Biochemistry of Obesity** 2 hours

The student should be able to

- Explain the factors that contribute to obesity.
- Explain the endocrine role of adipose tissue.
- Explain BMI.
- Name the adipokines.
- Relationship between leptin & adiponectin levels and adipocyte mass.
- Explain the role of leptin in regulating body mass.
- Explain the effect of leptin on orexigenic & anorexigenic neurons.
- Explain the relationship between adiponectin & metabolic syndrome.
- Explain the genetic factors contributing to obesity.
- Explain the consequences of the ob/ob homozygous condition.
- Explain the consequences of the db/db homozygous condition.

Clinical relationships.

- Explain the relationship between obesity & metabolic syndrome.

Total Lecture Hours **60 Hours**

Semester III

Lecture topics

1. **Biochemistry of Hormonal disorders** 6 hours

The student should be able to

- Describe the integration of different endocrine glands to perform function and control homeostasis.
- Discuss the major disorders associated with following endocrine glands.

  Pituitary
  Thyroid
  Adrenal
  Pancreas
- Explain the symptoms for the disorders associated with hormonal imbalance and their biochemical basis.
- Identify the metabolic alterations which lead to different types of DM.
- Explain the biochemical basis of insulin resistance.

Clinical correlations;

- Describe clinical significance of estimation of fasting, random, postprandial blood glucose, Oral Glucose Tolerance test (OGTT), glucose challenge test, fructosamine, HbA1c, C-peptide and Advanced glycated end products (AGE).
- Interpretation of laboratory reports.

2. **Xenobiotic/Liver metabolism** 4 hours

The student should be able to

- Define xenobiotics.
- Explain why the liver adopted special pathways to detoxify / eliminate xenobiotics.
- Explain the overall plan of the liver to deal with xenobiotics.
- Explain why the liver use enzymes of very low specificity to deal with xenobiotics.
- Discuss instances when the same pathways convert less toxic metabolites to toxic products.

- Outline the three phases of drug metabolism.
- Explain why the liver conjugates xenobiotics during its metabolism.
- Identify the compounds that the liver uses for conjugation.
- Outline the role of Cytochrome p450 enzymes in drug metabolism.
- Outline the three routs of metabolism of paracetamol.
- Explain how paracetamol is metabolized in the liver.
- Outline the metabolism of ethanol and methanol.
- Explain the liver function tests.

  Clinical correlations;
- Explain how constituents of cigarette smoke is converted to carcinogenic metabolites.
- Explain how paracetamol can become toxic.

3. **Biochemistry of Plasma protein and clinical applications.** 2 hours

   The student should be able to
   - List the main plasma proteins.
   - Explain the diagnostic values of plasma proteins.

     Clinical Correlations;
   - Identify serum electrophoretic patterns in diagnosing clinical conditions and interpret laboratory reports.

4. **Biochemistry of Adrenoceptors** 2 hours

5. Liver function/ profile test 2 hours

The student should be able to

- Describe what is included in a liver function / profile test.
- Describe the biochemical changes occurring in jaundice, cirrhosis and hepatitis.
- Differentiate the different types of Jaundice based on laboratory reports.
- Interpret liver profile reports.

6. Renal function/profile test 2 hours

The student should be able to

- Describe what is included in a renal function /profile test.
- Describe the clinical significance of glomerular filtration rate (GFR) and estimated glomerular filtration rate (e-GFR).
- Significance of serum creatinine and cystatin C, microalbuminuria, albumin/creatinine excretion ratio in urine.
- Know the significance of eGFR and urine protein excretion in diagnosis of chronic kidney disease (CKD).
- Know to interpret urine full report and renal function test report.

7. Nutrition

i. Vitamins as nutrient — 2 hours

The student should be able to

- Recall the discovery of vitamins.
- Define the terms vitamin, pro-vitamin and vitamer and state how a vitamin differs from a hormone and an enzyme.
- List the roles of vitamins.
- State the classification of vitamins.
- State food sources of fat soluble (A, D, E, K) and water soluble (B complex and C) vitamins.
- State the RDA of each fat- and water-soluble vitamins for infants /adolescents /adults/pregnant and lactating women wherever possible.
- Know the biochemical assessments for vitamin deficiencies.

ii. Fat soluble vitamins — 2 hours

Vitamin A

- Explain the sources of vitamin A, Bioavailability and RDA requirement
- Outline the transformation of pro-vitamin A to Vitamin A, absorption and transport of vitamin A from the intestine to
- liver and extrahepatic tissues.
- Explain the main biochemical and physiological functions vitamin A (role of vision cycle, influence of genomic expression of cell/protein synthesis, relationship between retinoids with cancer and immunity).
- Deficiency symptoms.
- Explain the Hypervitaminosis A.

Vitamin D

- Explain the sources of vitamin D, bioavailability and RDA requirement.
- Outline the synthesis of Vitamin D in the skin and absorption from the intestine.
- State the functions (calcium absorption and mineralization of bones, calcium and phosphate re-absorption).
- Deficiency symptoms (adults and symptoms).

- Explain the Hypervitaminosis D.

Vitamin E

- State the sources of vitamin E.
- Explain the role as an anti-oxidant and sparing action.
- State how the requirement is influence by vitamin A, intake of polyunsaturated fatty acids and advancing age.

Vitamin K

- State the sources of vitamin K
- Explain the biochemical functions of vitamin K dependent α carboxylase derive proteins (hemeostatsis and role in bone).
- State the actions of dicumorol and warfarin on vitamin K regeneration.

iii. Water soluble vitamins 4 hours

Thiamine (Vitamin B1)

- State the sources of vitamin B1and RDA requirements
- Effect of milling, extraction rate and cooking of serials on vitamincontent.
- State the biochemical functions (B1 dependent reactions in metabolism) and biochemical consequences in deficiency.
- State criteria are used to define thiamine states.
- Identify the symptoms of B1 deficiency.
- Outline the laboratory assessment of vitamin B1 deficiency.

Riboflavin (Vitamin B2)

- State the sources of vitamin B2 and RDA requirements
- State the biochemical functions (Biochemical role in cellular functions).
- Identify the deficiency symptoms.

Niacin (Vitamin B3)

- State the sources of vitamin B3 and RDA requirements
- State the biochemical functions.
- Explain the symptoms of Niacin deficiency and basis of mental depression in Pellagra and fatty liver.

Pyridoxine (Vitamin B6)

- State the sources of vitamin B6 and RDA requirements
- List naturally occurring pyridoxine derivatives.
- Describe the biochemical functions.

Folic acid (B9)

- State dietary sources and factors affecting folate absorption.
- List the biochemical functions.
- Explain folate and vitamin B12 deficiency and erythropoiesis.
- Outline the anti folates and principles of their action.

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Cobalamine (Vitamin B12)

- State the sources of vitamin B9 and RDA requirements
- State the role of GIF on B12 absorption.
- List the biochemical functions and effect of deficiency on the cell cycle.
- Explain the Deficiency symptoms (Pernicious Anaemia and Neurological symptoms).
- Distinguish folate and B12 deficiency.

Ascorbic Acid (Vitamin C)

- List the foods rich in ascorbic acid and factors affecting the absorption
- List the foods rich in ascorbic acid and factors affecting the absorption
- List the biochemical functions (Hydroxylation and other reactions, iron absorption and anti-oxidant functions).
- List the deficiency symptoms.
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iv. Minerals as nutrients 4 hours

a. **Introduction**

- State the mineral content of the body in terms of the fat-free body weight.
- List the seven “principle elements” and the “micro nutrient elements” essential to humans.

- Describe factors that can affect the absorption, retention, and availability of mineral nutrients.
- State good dietary sources requirements (infants, children, adults and for pregnant and lactating women, vegetarians) and functions of minerals stated below.

b**. Calcium**

- State the dietary sources and requirement
- Recall the normal ranges for serum Ca and phosphate and the formsin which Ca is found in serum.
- Recall the factors that influence Ca2+ absorption in the intestine and explain their mode of action.
- Explain the part played by calcitriol in "adaptation to a low Ca intake".
- Explain the deficiency diseases (a) rickets (b) osteomalacia.

c**. Iron**

- State the dietary sources and requirement
- List the different tissues in which iron is found, and the functions performed by iron in these tissues.
- List the factors that influence the absorption of dietary iron and explain their mode of action.
- Discuss iron absorption, transport and loss.
- Explain the diseases related to iron overload.
- Discuss the deficiency disease (stages of anaemia) & clinical symptoms and biochemical markers (TIBC, BI, PS, ferritin) and normal values.

d**. Iodine**

- State the dietary sources and requirement
- Outline the steps in thyroid hormone synthesis and role of iodine
- State the factors that (a) stimulate or inhibit (b) trapping of iodine to release of T3 and T4.32
- Explain the term iodine deficiency disorder (IDD) and endemic goiter.
- Recall that IDD should be prevented as early as possible in the reproductive life, preferable before conception, during pregnancy and early in infancy.

- Know how iodized salt need to be use and store and distributed in Sri Lanka.

e**. Zinc**

- State the dietary sources and requirement
- Explain the biochemical roles of Zn
- Discuss the deficiency disease & clinical symptoms.

f. **Fluorine**

- State the dietary sources and requirement
- Explain the function of fluorine in bone and teeth with special reference to prevention of dental caries.
- Outline the toxicity (dental fluorosis & osteofluorosis) &defluoridation of water.

g**. Selenium and Chromium**

- State the dietary sources and requirements
- State the relationship between selenium and chromium.
- Explain that selenium as an essential component of glutathione peroxidase.
- Outline the association between selenium and vitamin E
- Outline the association between chromium and GTF.

V. Foods of plant origin and animal origin 2 hours

- State why your body needs food
- Identify the major food groups origin in plant & animal

Origin in plant

Cereal Grains and Products
Pulses
Roots and Tubers
Fruits Vegetables
Nuts and Seeds
Plant-based Fat & Oil

Origin in animal

Fish & Seafood
Meat & poultry
Eggs Milk and milk products
Animal-based Fat & Oil

- Give the examples for each group.
- Describe nutritional composition in major food groups of animal/plant.
- Compare the bioavailability of plant foods vs animal foods.
- List the major health benefits which get from animal foods/plant foods.

vi. Energy and protein requirement

a. Introduction to nutrition and Energy of food 2 hours

- Understand the meaning of nutrition, nutrients, and food
- Explain "Why is it important for medical students to learn about nutrition"
- Recall how energy is used by humans (note; major protein Na/K pumps).
- Recall the sources of dietary energy and units of energy (kcal and J).
- Define the term 'Recommended Dietary Allowance' (RDA).
- Explain the terms 'gross energy' and 'metabolizable energy values of food.
- Define "Atwater factors" and calculate the energy value of food using the different values for macronutrients and alcohol

b. Energy requirements 2 hours

- Define respiratory quotient, specific dynamic action.
- Basal/resting metabolic rate (BMR/RMR) and state the conditions under which BMR are measured.
- Explain the effects of body size and composition, physical activity, hormones, gender and climate on energy expenditure.
- State the methods used in estimating energy requirements of an individual (BMR multiples depending on activity/ physical activity factors or equations with activity factors).
- Describe the energy and protein requirements in infant, child, adult elderly, pregnancy and lactation.(WHO & Sri Lankan recommended values)

c. Amino acids, Protein requirements and homeostasis. 4 hours

- Distinguish between indispensable, dispensable and conditionally indispensable amino acids.
- Compare the quality of proteins in commonly used foods in Sri Lanka.
- State the WHO definition of protein requirement of an individual, (a) an adult man (b) a pregnant woman (c) a lactating woman (d) pre-school child.
- Explain the term "nitrogen balance" and state the effect of energy intake on N balance.
- Explain the term "protein-sparing action" and the importance of this action
- State the mechanisms by which protein homeostasis is maintained during (a) amino acid imbalance (b) protein deficiency and (c) starvation.
- State the in vitro and in vivo methods that could be used for assessing the nutritive value of proteins ie. Biological value, true digestibility, net protein utilization, chemical score and compare the advantages and disadvantages of in vivo and in vitro methods.

d. Assessment of nutritional status 2 hours

- Outline methods of nutritional assessment (ABCD approach).
- Describe the anthropometric measurements used in assessing the nutritional status of adults (waist circumference, hip circumference, waist: hip, mid-upper arm circumference, BMI) and children (weight for height/weight for age/ height for age/ occipitofrontal circumference).

e. Energy protein malnutrition (EPM) 2 hours

- List the clinical signs and symptoms in kwashiorkor and marasmus and relate them to biochemical changes occurring in EPM.
- State the changes seen in plasma in (a) Kwashiorkor and(b) Marasmus.
- List methods of assessing EPM.

vii. Foods and Diet

a. Food groups 1 hour

- Identify the six food groups of Sri Lankan food pyramid
- Give the examples for each food groups
- Identify major nutrients in each food groups
- Know the meaning of "serving sizes"
- State the recommended no. of daily servings from each food groups

b. Diet and basic of diet formulation. 3 hours

- State factors that influence the nutritional requirements of individuals.
- State the principles behind formulating diets.
- State factors are considered when prescribing a diet for infants (principles of complementary feeding)/child/adult/pregnancy/lactation/elderly/athletes/
- State the dietary principles of managing metabolic diseases such as diabetes mellitus, CVD, CKD, and obesity.

Diabetes mellitus

- State the standard dietary requirements of a diabetic diet
- Explain the dietary guidelines for diabetic patients
- Explain the meal planning with Glycemic Index (GI) and Glycemic Load (GL)

Cardiovascular disease (CVD)

- State the standard dietary requirements of a diabetic diet
- Explain the dietary guidelines for diabetic patients

Chronic kidney disease (CKD)

- State the standard dietary requirements of a diabetic diet
- Explain the dietary guidelines for diabetic patients
- Understand the principle behind the restriction of protein and certain minerals in the diet of CKD patients

Obesity

- State the standard dietary requirements for weight management
- Explain the dietary guidelines for obesity condition

c. Functional Food 1 hour

- Explain what are functional foods, nutraceuticles, probiotics and prebiotics.
- Understanding of functional foods and their role in promoting health
- Explain the functional foods commonly encountered in the diet, their bioactive compounds and the nutrition and health role.
- Provide understanding of the basic scientific principles necessary to evaluate benefits of and claims for nutraceuticals and functional foods

8.Molecular and Precision Approaches in Medicine

i. Principles and importance of molecular and precision approaches in medicine. 2 hours

Students should be able to

- define the terms used in molecular and precision approaches in medicine.
- explain the principles and importance of molecular and precision approaches in medicine.

ii. Molecular techniques in medical practices. 4 hours

Students should be able to

- describe the basis and applications of molecular techniques in medicine: PCR, DNA sequencing (Sanger, and high-throughput sequencing techniques -NGS (GWS, RNA-seq), RFLP, Hybridization (northern, southern and western blotting techniques), ELIZA, Immunofluorescence (IF) /Immunohistochemistry (IHC).

iii. Genetic engineering in medical practices. 4 hours

Students should be able to

- describe the basis and applications of genetic engineering in medical sciences: recombinant DNA technology and its applications, vaccines, gene therapy and gene editing with CRISPR/Cas9

iv. Molecular biology of cancer. 6 hours

Students should be able to

- explain the molecular basis of cancer and identify the hallmarks of cancer.
- explain the role of oncogenes and tumor suppressor genes in oncogenesis.
- describe the significance of tumor markers in disease diagnosis and prognosis and list commonly used tumor markers (ovary, breast, prostate, colon, liver, bone).
- interpret laboratory reports in cancer diagnosis.

v. **Introduction to precision approaches in cancer treatment. 6 hours**

Students should be able to

- explain OMICs-based biomarkers (genomics, transcriptomics, epigenomics, proteomics, metabolomics, pharmacogenomics).
- describe targeted cancer therapy and its challenges.
- describe immunotherapies and its challenges (T-Cell transfer therapies: CAR-T cell therapy in cancer treatment).

Total Lecture Hours 60 Hours

SUMMARY OF EXAMINATIONSFORMAT

Exam structure

Component	**MCQs**	**SEQs**
End Semester Examination I	15 (45 minutes)	2 (40 minutes)
End Semester Examination II	15 (45 minutes)	2 (40 minutes)
End Semester Examination III	15 (45 minutes)	
Final Examination (Written)	40 (120 minutes)	5 (150 minutes)
OSPE	20 stations (60 minutes)	
Viva Voce	10 minutes	

Marks Percentages

Component	**Proper**	**Repeat**
End Semester Examination I	5%	-
End Semester Examination II	7.5%	-
End Semester Examination III	7.5%	
Written (MCQs + SEQs)	60%	70%
OSPE	10 %	20%
Viva voce	10%	10%
Total	**100**	**100**