Rawalpindi Medical University

CURRICULUM

PhD in Chemical Pathology

2023

CONTENTS

INTRODUCTION

This curriculum is developed for MPhil training in Chemical and Molecular Pathology. It outlines the curricular goals, objectives, curricular strategies and assessments of trainees in Chemical and Molecular Pathology. It mentions the core, system based and procedural skills competencies and discusses the essential principles for the training program. There is also information about the institution, faculty, credit hours, courses and induction of trainees, teaching strategies, assessment, evaluation processes, weekly schedules, certification and accreditation.

Chemical and molecular Pathologist produce and interpret the results of chemical and biochemical analyses performed on blood and other body fluids to help in the diagnosis and management of disease. Increasingly their work includes selected population screening and they advise on planning and monitoring treatment. Those who choose Chemical and Molecular Pathology normally work in a hospital laboratory / Pathology Department/Molecular Diagnostics and analyses low concentrations of substances in patients 'blood and other fluids to aid clinicians in the diagnosis of disease and in monitoring its course during treatment**.**

1.1 Program Mission

The mission is learning the essential and fundamental concepts of Chemical and molecular Pathology during training and carry out extensive research in new areas. The aim is to build in students, essential skills to pursue rest of duration of training as life-long self-directed learner under guidance of his / her supervisor.

1.2 Overall Goals of Curriculum of Chemical and Molecular Pathology

The overall goals of a training program should be to develop a pathologist with the following characteristics.

a. Acquires appropriate integrative knowledge of Chemical and molecular Pathology of common diseases and is able to put his theoretical knowledge for clinical problem solving.
b. A molecular pathologist must understand methods of diagnostic/genetic test development, test utilization in the context of both generally applicable and patient-

specific clinical settings, and assay interpretation in the acute and chronic clinical management of patients. The specific level of technical expertise must be attained during training in various sub disciplines in chemical pathology.

c. The pathologist must understand the science and technology of the clinical laboratory and assures the quality, clinical appropriateness, and usefulness of the data produced by that laboratory.
d. A pathologist must understand the role of research in clinical decision-making, test development, knowledge generation, and continuing education. Becomes aware of the important gaps of knowledge in the field in order to define some areas for future research.

1.3 Compulsory Core Courses and Lab Rotations

Course core will cover a significant part of Chemical Pathology along with essential components of Molecular Pathology. Generally, these courses will be covered in first year of the programme. At the end of training programme the trainee should be able to:-

a. Carry out the correct technique of collection & handling of various specimens
b. Comprehend the significance of patient preparation, sample requirement for a particular test & analyte stability to produce quality results
c. Operate independently instruments & procedures used in chemical pathology lab.
d. Perform different assays on semiautomatic & automatic instruments with achievable analytical accuracy & reproducibility
e. Understand and implement quality control procedures in the lab
f. Interpret critically the results of lab investigations in the context of the clinical profile
g. Do trouble shooting of pre-analytical, analytical and post-analytical error
h. Carry out lab management including development of SOPs.
i. Clinical application of molecular genetics.
j. Overview of medical genetic disorders taught at a level suitable for those preparing for certification examinations in Molecular biology and clinical genetics specialties or for those whose research focus or clinical practice will have a strong emphasis in medical genetics.
k. The principles of genetics and genomics related to medical genetics and how it is integrated into clinical practice.

1.4 Program over view

The program is designed to produce doctors with adequate basic knowledge and skills required for working in a Chemical Pathology Section/Applied Genetics/Molecular diagnostics of a Hospital Laboratory, who are able to correlate their findings with underlying pathogenic mechanisms, able to advise and perform correct diagnostics procedures, develop the ability to communicate effectively and learn independently using computer and internet.

1.5 Rationale

There is a shortage of training programs with clearly defined learning outcomes/ objectives for post graduate Chemical Pathology and molecular Pathology Education in Pakistan. The suggested programme will help mitigate the acute shortage of Chemical Pathologists. It will also help in producing research scholars of international standard which can become useful members of the teaching faculties of various Medical Colleges and Universities. These experts will also contribute in training of laboratory technologists and junior doctors and bring about improvement in medical diagnostics.

1.6 Curricular Perspective

Curriculum will be outcome based with constructivist approach keeping in mind the principles of adult learning. The faculty development and capacity building will be carried out by organizing workshops on modern teaching methodologies. It will be mandatory for the faculty to attend workshops on Education Planning, Assessment of Competence and Supervisory Skills as well as Research Methodology arranged by RMU or other collaborating institutes.

1.7 Education Strategy

SPICES strategy will be used for curriculum implementation. Different aspects of the SPICES model will be adopted to variable degree for this training course. The six concepts in the SPICES model used are as following:

a. **S**tudents centered (30%) vs Teacher centered Teaching (70%): Study guides and educational resources will be available to help, and give activities to help students understand and remember the material. Curriculum will be made as adaptive as possible which will allow working collaboratively with everyone involved.

b. **P**roblem based (60%) vs Information gathering (40%) : Problem based learning will be used in most of the curriculum by using real world clinical scenarios. This will help preparing students for clinical practice so as to encourage early development of decision making skills, a holistic approach to clinical problems, and the development of team working skills.

c. **I**ntegrated (20%) vs Disciplined base (80%) : In higher postgraduate courses integration cannot be practiced so that students may develop a clearer picture of a discipline as a career in the discipline based method. However, some steps will be taken e.g. Problem based learning, Task based learning, "Hot case" learning, spiral curriculum and multi-professional learning.

d. **C**ommunity based (10%) vs Hospital based (90%) : Students will learn some aspects of the specialty in community based settings e.g. population based screening of diabetes mellitus.

e. **E**lectives with a core (10%) vs Uniform elective (90%) : Some time will be spared for trainees study extra topics or subjects of their own choosing including biostatistics and research methodology.

f. **S**ystematic (80%) vs Apprenticeship(20%) approach : The curriculum will made more systematic by making it outcome based i.e. student learning is focused on predefined learning objectives. Moreover a curriculum map will be defined which is a comprehensive approach of defining what is taught, how it is taught, when it is taught, and when it is assessed or examined. The curriculum map makes the curriculum transparent to all students, teachers, and the public. Areas in a curriculum map include the expected learning outcomes, the curriculum content or required areas of expertise, assessment procedures, learning opportunities, learning resources, a timetable, the staff involved, and measures for future curriculum development.

2. Entry Criteria and Selection Methodology

a. Candidates will be selected on open merit through advertisement in the national newspapers. The applicants have to take an GRE subject test or University test as per guidelines of HEC and successful candidates will then appear in an interview. The main objective would be to assess their prior basic scientific and general knowledge and assessment of their learning style and computer skills.

b. The selected trainees must have their own laptop computer and digital scientific calculator to record data. They will be sent curricular guidelines, basic course material and the suggested text books with identified pages to study before they start formal training. The curricular guidelines will provide clear statements of what students are supposed to learn and achieve and how they are going to be assessed.

c. Number of total trainees will be determined keeping in mind the number of supervisors present in each department at the time of induction. A ratio of trainer to trainee of FOUR per year will be maintained.

4.0 Faculty

The faculty will consist of full time supervising consultants who are certified supervisors of HEC and RMU. All supervisors will be registered with RMU on the basis of following criteria:

a. Higher Post-graduate Qualification e.g. PhD

b. Post-graduate (PhD) experience of at least five years

5.0 PROGRAM STRUCTURE

Duration of Course:

Medical Graduates: Four years

FCPS (Chem Path/Biochemistry) qualified medical graduates: Three Years

MPhil (Chem Path/Biochemistry) qualified medical graduates: Three Years

Students' Level

For Medical Graduates

- Qualifications MBBS
- Experience 1-Year House Job

For FCPS and MPhil Qualified Medical Graduates

- Qualifications MBBS
- FCPS (Chem Path/Biochemistry) and/or MPhil (Chem Path/Biochemistry)
- Experience
  - 1-Year House Job
  - 2 Years post FCPS or MPhil working experience in a diagnostic laboratory and/or a Medical College.

Minimum GPA Requirement. For admission in PhD programs, a minimum CGPA of 3.0 (out of 4.0 in the semester system) or First Division (in the annual system) in the most recent degree obtained is required, whether such was degree obtained from Pakistani or foreign universities.

Statement of Purpose. As part of the application for admission to PhD programs, applicants shall be required to submit a statement of purpose, which shall form an integral part of the application. The admissions committee shall use the information provided to ascertain the preparedness and interest of the candidate in pursuing doctoral studies

6.0 Venue

RMU and Allied Hospitals (Rotation in COMSATS, KRL, AFIP and Quaid-e-Azam University Islamabad)

8.0 Logistics

a. Learning Resource Centers and multimedia and other learning aids.
b. Computers with internet connections in the department

9.0 MODES OF INFORMATION TRANSFER

LEARNING OUTCOMES		M.I.T (1)	M.I.T (2)
1.	Describe and correlate various principles of Clinical Chemistry	Structured Lectures	Small group discussion (SGD), Journal Club Meetings (JCM)
2.	Differentiate characteristics of various laboratory techniques	Skill Lab Session	SGD, JCM
3.	Describe Quality Assurance and Lab Statistics	Skill Lab Session	SGD
4.	Describe methods of various analytes e.g. glucose, Hb and Staining	SGD	JCM, Clinico-Pathological Conference (CPC)
5.	Analyze and interpret laboratory data in various systems	Skill Lab Session	JCM, CPC On the job training (OJT).
6.	Able to use and maintain basic laboratory instruments	Skill Lab Session	SGD
6.	Students should be able to perform various laboratory tests e.g. estimation of drugs	Skill Lab Session	OJT i.e. performing tests on patient samples after they have been reported.
7.	Perform basic statistical tests used in Chemical Path lab in routine e.g. Calculation of mean, SD and CV	SGD	OJT i.e. assisting in routine statistics under supervision.
8.	Use of computer and IT skills in laboratory	Laboratory Skill Session	OJT under supervision.
9.	Carry out counseling, showing professionalism and following principles of laboratory safety	PAL, Role Play	OJT under supervision, video clips (especially for lab safety)
10	Describe basic aspects of molecular genetics.	Structured Lectures	Small group discussion (SGD), Journal Club Meetings (JCM)
11	Should be able to forges a link between genotype and phenotype and covers topics in contemporary genetics, including Mendelian	Structured Lectures	Small group discussion (SGD), Journal Club Meetings (JCM)

	analysis, chromosomes, mitosis/meiosis, recombination, mutations and mutagenesis, linkage mapping, complementation, extranuclear inheritance, genetic interactions and epistasis, epigenetics, and developmental genetics.		
12	Exploration of several new technologies for determining gene function on a genome-wide scale and for integrating information into a systems-level view of biological processes.	Laboratory Skill Session	OJT under supervision.
13	Describe the principles of genetics and genomics related to medical genetics and how it is integrated into clinical practice.	Structured Lectures	Small group discussion (SGD), Journal Club Meetings (JCM)
14	Discuss traditional mitochondrial diseases (e.g., caused by mutations in the mitochondrial DNA); more recent findings of involvement of mitochondria in pathologies such as cancer, diabetes, aging, and neurodegenerative diseases.	Structured Lectures	Small group discussion (SGD), Journal Club Meetings (JCM)

10.0 Credit Hours

a. One-hour Small Group Discussion (SGD) Session, Seminar or quiz per week for 16 weeks or 2 SGD Sessions per week for 8 weeks

Or

b. Two hours Skill Lab Training Session, slide session, on job training or Clinical work per week for 16 weeks or four hours Skill Lab Training Session, slide session, on job training or Clinical work per week for 8 weeks

PHD PROGRAMME

1	**Degree Offered**	**Duration (Credit Hrs)**
	a. For Medical Graduates (4 years)	78
	b. For MPhil qualified (3 years)	48
2	**Course Work**	
	a. Major Subject(Compulsory core course) Lectures/Tutorials/Seminars Experimental Work Advanced Experimental Work	24
	b. Allied courses, Biostatistics, Research Methodology, Lab Techniques/Instrumentation Lectures/Tutorial/Seminars Experimental Work	06
3	**Advanced course work of major subject for PhD candidates**	**18**
4	****Research Work and Thesis**	
	PhD	30

COURSES AND LAB ROTATION IN CHEMICAL & MOLECULAR PATHOLOGY

CODE **YEAR-1** **Semester-1**	**COURSES**	**CREDIT Hours**
CHP-010	Basic Laboratory Principles	1
MP-010	Basic Molecular Pathology and Genomics	2
CHP-011	Pathophysiology	2
CHP-012	Biochemical Analytes	2

CHP-013	Major Biochemical Assay Methods: Lab-I	2
ASC-010	Research Methodology	1
Semester-2		**10 credits= 18 weeks**
CHP-014	Analytical techniques & Instrumentation	2
MP-011	Laboratory Techniques in Molecular Diagnostics Lab-I	1
CHP-015	Instrument handling: Labs -II	2
CHP-016	Clinical Endocrinology	2
MP-012	Basic Medical Genetics	2
ASC-011	Data Interpretation	1
Semester-3		**10 credits= 18 weeks**
MP-013	Molecular Pathology of Mitochondrial Disease	2
CHP-017	Quality Management	2
MP-014	Metabolism and disease	2
ASC-012	Biostatistics/Seminar-1	1
ASC-013	SPSS Data Analysis	1
ASC-014	Animal Handling	2
Total Credit Hours		**10+10+10=30**

CODE Year-2	COURSE	CREDIT HRS
Semester-3		**16 weeks=9 credits**
MP-020	Advanced Topics in Molecular Biology & Cellular Signalling	2
MP-021	Medical Genetics and Pediatric clinical chemistry	2
CHP-021	Toxicology and therapeutic drug monitoring	2
CHP-022	Advanced Analytical techniques Automation and POCT	2
MP-023	Advance Molecular biology Techniques Lab-II	1
Semester-4		**16 weeks=9 credits**
CHP-023	Advanced Biochemical Assay methods-Lab-II	1
MP-024	Current Advances in Molecular Biology and Molecular diagnostics	2
CHP-024	Laboratory Management and Quality Assurance	2
CHP-025	Literature search/Medical synopsis writing	2
CHP-026	Seminar	2
Total Credit hours		9+9=18

iv. CHP-030:
Research Work and Thesis **Credit Hours**

A. PhD **30**

Medical Knowledge

- Develop and maintain knowledge in the basic and clinical sciences necessary for effective consultation in laboratory medicine.
- Demonstrate sufficient knowledge to determine clinically optimal cost-effective testing and laboratory-based strategies, including issues of turn around time, test menu construction, and in-house vs referral diagnostic testing.
- Recognize the unique aspects of laboratory medicine practice as modified by patient age and other patient population characteristics, especially of pediatric and geriatric practice.
- Demonstrate awareness and understanding of general and test-specific standards for method development and evaluation.
- Employ mathematics and statistics as appropriate to laboratory testing; understand and implement quality control (QC) and quality assurance procedures as required.
- Demonstrate awareness and understanding of proficiency programs.
- Demonstrate knowledge of the principles of clinical research design, implementation, and interpretation.
- Be able to design a study that can be used to validate methodologies and parameters of clinical utility for the implementation and continuing use of new evidence- based analytes in the local setting.

Evidence-based Medicine

- Demonstrate knowledge of evidence-based medicine and apply its principles in practice.
- Use multiple sources, including information technology, to optimize lifelong learning and support patient care decisions.
- Develop personally effective strategies for the identification and remediation of gaps in medical knowledge needed for effective practice.

- Use laboratory problems and clinical inquiries to identify process improvements to increase patient safety.
- Demonstrate the ability to critically assess the scientific literature.

Patient Care

- Gather essential and accurate information about patients using all relevant available modalities.
- Act as a skilled consultant to other clinicians to develop a diagnostic plan based on specific clinical questions and relevant clinical and pathologic information.
- Provide expert consultation on the interpretation and follow-up of unusual or unexpected test results.

Point-of-Care Testing

- Understand definitions of POC and the range of analytes available in devices used at the point of care.
- Understand the principles of performance for common POC tests such as glucose, urine drugs of abuse, rapid microbial antigen, and activated clotting time. Under stand the performance characteristics of the common POC devices used for these tests. Know the issues surrounding specimen collection and preparation and the limitations and interpretation of results
- Understand the differences in reference ranges and test performance characteristics between POCT and laboratory assays.
- Be able to assess economic, workflow, human resources, and clinical factors driving the decision to perform testing at the point of care vs the central laboratory.

Communication Skills

- Demonstrate the ability to write an articulate, legible, and comprehensive consultation note. Provide a clear and informative report, including a precise

diagnosis whenever possible, a differential diagnosis when appropriate, and recommended follow-up or additional studies as appropriate.

- Demonstrate the ability to provide direct communication to the referring physician when interpretation of a laboratory assay reveals an urgent, critical, or unexpected finding.
- Conduct both individual consultations and presentations at multidisciplinary conferences.
- Choose effective modes of communication (listening, explanatory, questioning) and mechanisms of communication (face-to-face, telephone, e-mail, written), as appropriate.
- Demonstrate skills in obtaining informed consent, including effective communication to patients about procedures and possible complications.
- Demonstrate skills in educating colleagues and other healthcare professionals:
- Demonstrate the ability to present laboratory medicine concepts effectively in continuing education settings and in the day-to-day laboratory environment.
- Demonstrate an understanding of the principles one must follow when educating other practicing pathologists through publications or seminars on new testing and research discoveries.

Professionalism

- Demonstrate positive work habits, including punctuality, dependability, and professional appearance.
- Demonstrate a responsiveness to the needs of patients and society that supersedes self-interest.
- Demonstrate principles of confidentiality with all information transmitted both during and outside of a patient encounter.
- Demonstrate knowledge of regulatory issues pertaining to the use of human subjects in research.
- Demonstrate a commitment to excellence and ongoing professional development.
- Demonstrate interpersonal skills in functioning as a member of a multidisciplinary healthcare team.

Laboratory Management

- Demonstrate understanding of the role of the clinical laboratory in the healthcare system.
- Demonstrate the ability to design resource-effective diagnostic plans based on knowledge of best practices in collaboration with other clinicians.
- Demonstrate knowledge of basic healthcare reimburse ment methods.
- Demonstrate knowledge of the laboratory regulatory environment, including licensing authorities.
- Understand and implement policies to continually improve patient safety as they relate to clinical laboratory testing at all levels.

COURSES CODE: CHP-010

BASIC LABORATORY PRINCIPLES (CREDIT HRS 01)

Basic Laboratory Techniques and Equipment

Components, principles, operation and maintenance of basic laboratory equipment including centrifuge balances, automatic pipettes, water bath, incubators, refrigerator, freezer, glass and plastic ware, deionizer, distillation plant etc. Basic concept of SI units, conversion factors from old system of units to SI units, units in clinical enzymology and standardized reporting of lab results.

Concept of solute and solvent

- Expressing concentrations of solutions

Units of measurement

- International system of units
- Conversion rules
- Standardized reporting of test results

Chemicals and reference materials

- Reagent grade water
- Chemical reagents
- Reference material

Basic techniques and procedures

- Volumetric sampling and dispensing
- Analytical Weighing
- Centrifugation
- Buffer solutions
- Preparation of solutions
- Thermometry/water bath/refrigeration

Specimen Collection and Handling

The course include requirements for request forms, collection of blood & various body fluids description of vacuum tubes used for phlebotomy, effect of anticoagulants, stability studies and interference studies. Physiological and biological factors affecting the analytes

Specimen collection and processing

- Blood
- Urine
- Feces
- Spinal fluid
- Synovial fluid
- Amniotic fluid (Amniocentesis)
- Pleural pericardial and ascetic fluid

Handling of specimens for testing

- Maintenance of specimen identification
- Separation and storage of specimens
- Transport of specimens

Hazards in chemical pathology lab and safety procedure

The course includes hazards from dangerous chemical, infection hazards, apparatus and building hazards, with special emphasis on safety guidelines procedures and first aid treatment

Lab safety

- Safety equipment
- Safety inspections
- Hazards plans

COURSES CODE: MB-010

❖ **BASIC MOLECULAR BIOLOGY AND GENOMICS (CREDIT HRS 02)**

. Forges a link between genotype and phenotype and covers topics in contemporary genetics, including Mendelian analysis, chromosomes, mitosis/meiosis, recombination, mutations and mutagenesis, linkage mapping, complementation, extranuclear inheritance, genetic interactions and epistasis, epigenetics, and developmental genetics.

COURSES CODE: CHP – 011

❖ **PATHOPHYSIOLOGY (CREDIT HRS 02)**

Cardiovascular Diseases and Lipids

The course will include cardiac biomarkers and biochemistry of plasma lipids, lipoprotein metabolism. Classification of lipid disorders, investigation of lipid disorders and current recommendations on detection of lipemia. Clinical significance of lipoproteins and hyperlipoprotenemia.

Renal function and diseases

The course includes renal physiology, clinical syndromes associated with kidneys, acute and chronic renal failure, ureaemia and nephrotic syndrome. With special emphasis on pathophysiology and investigations of renal disease, oliguria, polyuria, renal calculi, urate metabolism, hyperuricemia, gout and hyperuricemia, clearance studies, dialysis and renal transplantation

Electrolyte and Water Metabolism

Including water and sodium balance and hormones associated with it i.e. aldosterone, Renin Angiotensin and Antidiuretic, relation between hydrogen and potassium, disturbances & investigation of water and electrolyte balance and urinary & intestinal losses.

Acid Base Balance and Blood Gases

Hydrogen ion homeostasis, buffer systems, disturbances of hydrogen ion and investigations of acidosis and alkalosis, Arterial pH and pCO_2 estimations acid base balance disturbances

Liver and Gall Stones

Function of liver, disease of liver with special emphasis on hepatitis, Cirrhosis, Cholestasis and liver failure, Bilirubin, jaundice and metabolic disorders of liver, formation and detection of Bile acids and gall stones

Intestinal Absorptions; Gastric and Pancreatic Functions

Normal digestion and absorption including gastric & pancreatic function special emphasis on differential diagnosis and investigation of malabsorption syndrome, steatorrhoea and failure of absorption of specific substances

Disorder of bones

Factors effecting total plasma calcium, parathyroid hormone, calcitonin, vitamin D, disorders of calcium metabolism, hypocalcemia and hypercalcinemia

COURSES CODE: CHP-012

❖ BIOCHEMICAL ANALYTES (CREDIT HRS 02)

- **Protein**

Amino acid and aminoaciduria's. Plasma protein, inflammatory response, acute phase proteins, immune response, disorders of B-cells & T-cells, immunoglobulins and complement proteins. Indications of protein, albumin & globulin estimation, protein electrophoresis normal pattern and changes in disease states will be included. Serum and fluid protein and amino acid assessment. Methods of assessing proteins in serum urine and other body fluids

- **Renal Function Test**
  - Assessment of renal function, Serum creatine, urea, uric acid
  - Assessment of kidney function: estimation of glomerular filtration rate
- **Liver Function test**
  - Assessment of liver disorders
  - Estimation of bilirubin transaminase, LDH, CK, CKMB, ALP, ACP, GGT, cholinesterase, acid phosphatase and amylase in serum and other body fluids
  - Assessment of gastric, pancreatic, and intestinal function
- **Cardiac and Lipid**
  - Measurement of cholesterol, triglycerides, HDL-C, LDL-C, and apoliproteins with special emphasis on standardization.
  - Assessment of Cardiac biomarkers
  - Assessment of BNP/homocystine/C-reactive protein
- **Electrolytes**
  - Water and electrolyte disorders
  - Measurement of serum Electrylytes
- **Acid Base**
  - Blood Gas estimations
  - Assessment of acid base disorder : blood gases and oxygen saturation

- **Calcium, Phosphate and Magnesium**
  - Tests for diagnosis of calcium of phosphate and magnesium disorders

- **Tumor biomarkers**

Definition, classification and distribution of tumour markers, proteins, enzymes, hormones, oncofetal tissue, non hormonal antigens, carbohydrates etc. hormonal effect of tumours in non endocrine tissue, non hormonal peptides as indicator of malignancy, desirable features of a tumour marker, clinical usefulness and tests for common tumour markers e.g. AFP, CEA, HCG, PSA, HIAA, HVA, CA125, CA199 catecholaminers and immunoglobulins. It includes Clinical applications of:

  - Enzymes
  - Hormones
  - Oncofetal antigens/Beta HCG/AFP/CEA/PSA
  - Cytokeratins
  - Carbohydrate markers
  - Proteins
  - Genetic markers

- **Haemoglobin Iron, and bilirubin**

The course includes biosynthesis of haemoglobin, disorders of Haem synthesis, various type and investigations of porphyrias, Iron metabolism, absorption, excretion and transport, factors effecting plasma iron concentration, estimation of serum iron, TIBC, ferritin and investigation of anaemia.

- **Vitamin assessment**
  - Vitamins
  - Vitamins A, D, E, K
  - Vitamins B_1, B_2, B_6
  - Vitamin B_{12}
  - Vitamin C
  - Folic acid

COURSES CODE: CHP – 013

❖ **MAJOR BIOCHEMICAL ASSAY METHODS: Lab-II (CREDIT HRS 02)**

- **End Point Assay**
  - Determination of Blood glucose
  - Determination serum triglyceride
  - Determination of serum cholesterol/Lipoproteins
  - Determination total plasma proteins, albumin and globulin
  - Determination of serum urea
  - Determination of serum uric acid
  - Determination of serum/Urinary Creatinine clearance
  - Determination of Serum Bilirubin
  - Determination of Serum/Urinary Calcium
  - Determination of serum/urinary phosphorus
  - Determination of serum /Urinary Chloride
  - Estimation chloride
- **(ISE/ABG/Osmometry**
  - Ion selective Na+, K+, Cl+, pH, pO2, pCO2
  - Other ISEs, e.g. Ca2+, NH+4
  - Arterial Blood Gasses
- **Enzymology / Substract Chemistry**
  - Kinetic assays
  - Determination of serum Aspartate/Alanine Transaminase
  - Determination of serum lactate dehydrogenase
  - Determination of serum creatine phosphokinase
  - Determination of serum Alkaline Phosphatase
  - Determination of serum amylase

- **Immunoassay**
  - ELISA /Competitive immunoassay
  - Immunoradiometric assays
  - Chemiluminescent immunoassays
- **Immunochemical techniques (Protein chemistry)**
  - protein and urine electrophoresis
  - Immuinoeletrophoresis /Immunofixation
  - Immunonephelometry/Turbidimetry
  - Immunodiffusion
- **Miscellaneous**
  - Faecal occult blood
  - faecal fat
  - analysis of calculi

COURSES CODE: CHP–014

❖ **ANALYTICAL TECHNIQUES & INSTRUMENTS (CREDIT HRS 03)**

- **Instrumentation**

Description of features, principles working and maintenance of major instruments, comparison of different instruments and criteria for selecting an analyzer according to work load, utilization of reagents, technologists available and labour costs with special emphasis on different techniques in spectrophotometery, mass spectrometry, flourometry, nephrelometry, turbidemetry, electrolyte analyzer, acid base & gas analyzers, electrophoresis, chromatography, radioimmunoassay, ELISA and PCR

- Optical techniques
- Spectrophotometry/Photometry
- Fame emission & Atomic absorption Spectrophotometry
- Potentiometer/Voltametery/ ion-selective electrodes
- Arterial blood gas analysis
- Nephelometry and Turbidimetry

- Fluorometry / Phosphorescence
- Chemiluminescence, bioluminescence and electrochemiluminescence
- Electrophories
- chromatography & Planar chromatography
- Column chromatography & HPLC
- Gas chromatography & Mass spectrometry
- Principles of clinical Enzymology
- Principles of immunochemical techniques
- Automation in the clinical laboratory

COURSES CODE: MB-011

LABORATORY TECHNIQUES IN MOLECULAR DIAGNOSTICS

(CREDIT HRS 02)

- PCR
- BLOTTING TECHNIQUES

COURSE CODE:CHP-015

INSTRUMENT HANDLING LAB-II

- Preparation of Type 1 & Type 11 water
- Washing of glass ware
- Use of Balances and weighing
- Use of Pipettes & Volumetric Glass are
- Use of Centrifuge/filtration
- Measurement of pH and buffer solutions
- Visible & UV Spectrophotometer
- Flame Photometer/ISE Instruments
- Fluorometer/Chemiluminescence Instruments
- Arterial blood gas analysis
- Auto analyzer Programming
- Atomic absorption spectrophotometer
- ELISA/Immunochemical Quantitative analysis

- Electrophoresis operation
- TLC, HPLC & GC analysis

COURSES CODE: CHP – 016

❖ **CLINICAL ENDCRIONOLOGY (CREDIT HRS 02)**

With special emphasis on general endocrine functions, hormones and their mechanism of action, regulation and receptors. The endocrine functions and regulation of hypothalamus, pituitary gland, adrenal cortex, thyroid, parathyroid and gonadal hormones, assessment of pituitary, adrenal and thyroid functions by dynamic function tests. Affects of abnormal levels of cortisol, aldosterone, rennin Angiotensin, catecholaminers, serotonin, thyroid, clinical usefulness of urinary free cortisol, testosterone, DHEAS, androstendedione, sensitive TSH and free T4 and T3 tests, stimulation and suppression test, laboratory investigation of patients with hypothyroidism, hyperthyroidism, Cushing's syndrome, Addison's disease, Conn's syndrome, pheochromocytoma, hirsutism, infertility, congenital adrenal hyperplasia and prolactinoma.

❖ **Carbohydrates and diabetes**

- The course includes carbohydrate metabolism, maintenance of extra cellular glucose, hormones concerned with glucose metabolism with special emphasis on insulin. The disorders of carbohydrate metabolism, hyperglycemia, diabetes mellitus and hypoglycemia. Investigation of disorder of carbohydrate metabolism, estimation of glucose in serum and other body fluids, Glycosylated Haemoglobin, Insulin and insulin antibodies, inborn errors of metabolism, Glycogen storage diseases.
- Glucose homeostasis; role of insulin and counter regulatory hormones
- Classification and diagnosis of diabetes; glucose loading tests; glycosuria; gestational diabetes; insulin resistance
- Etiology of diabetes; genetic susceptibility; islet cell antibodies
- Complications; diabetic ketoacidosis; lactic acidosis, hyperosmolar and hypoglycaemic coma; nephropathy; lipid abnormalities
- Monitoring of diabetic control; home monitoring with reagent pad tests and meters; glycosylated hemoglobin and proteins; fructosamine
- Microalbuminuria and other laboratory investigations for monitoring of diabetic control
- Treatment of diabetes

- Causes and laboratory investigation of hypoglycaemia
- Inborn errors of carbohydrate metabolism

❖ **Normal physiology and biochemistry of hormones**

- Normal physiology, Synthesis, secretion, transport, Hormone receptors and mechanisms of action of steroid and protein
- Hypothalamus. The role hypothalamic releasing factors; somatostatin General feedback mechanisms and endocrine control

❖ **Pituitary**

- Pituitary. Physiology and pathology of the hormones of the anterior and posterior lobes
- Growth hormones; somatotropin
- Acromegaly; pituitary dwarfism and prolactinorma
- Dynamic function tests
- Isolated pituitary hormone deficiencies and pan hypopituitarism
- Diabetes insipidus, water deprivation

❖ **Thyroid**

- Thyroid function tests
- Hyperthyroidism/hypothyroidism
- Congenital hypothyroidism and screening programmes; hypothyroidism and goiter
- Thyroid autoimmunity
- Carcinoma of the thyroid

❖ **Adrenal Cortex**

- Adrenal function tests
- Cushing's syndrome; Interpretation of plasma cortisol, urinary free cortisol, ACTH assay
- Addison's disease
- Congenital adrenal hyperplasia
- Adrenal hyperplasia, Conns syndrome low renin hypertention

❖ **Reproductive endocrinology**

- Gonads physiology and function

- Investigation and management of female infertility
- Investigation of male infertility
- Pregnancy tests; test of feto placental function; Ectopic pregnancy ‘s
- HRT. Ectopic hormones

❖ **PTH: Calcium and bone metabolism**

- Physiology of calcium phosphate and magnesium
- Causes and investigation of hyper and hypo calcaemia
- Hyper parathyroidism; hypo parathyroidism; Renal osteodystrophy
- Osteoporosis; osteomalacia; Paget’s disease
- Disorders of phosphate homeostasis
- Disorders of magnesium homeostasis
- Urinary and blood Bone markers

COURSE CODE: MB – 012

BASIC HUMAN GENETICS

❖ Genome structure

❖ Regulation of Gene expression

❖ Recombinant DNA Technology

❖ Gene Mutation

❖ Oncogenes and Tumor suppressor genes

❖ PCR and blotting techniques

❖ Genetic counselling

COURSE CODE: MB-013

MOLECULAR BIOLOGY OF MITOCHONDRIAL DISEASE

Mitochondrial structure and function; mitochondria as sites of phenomena such as cell death, generation of free radicals, and production of most cellular energy. Traditional mitochondrial diseases (e.g., caused by mutations in the mitochondrial DNA); more recent findings of involvement of mitochondria in pathologies such as cancer, diabetes, aging, and

neurodegenerative diseases.

COURSES CODE: CHP – 017

❖ **QUALITY MANAGEMENT (CREDIT HRS 02)**

There will be special emphasis on concept of quality control (QC). Explanations of terminology used in QC e.g. accuracy precision, specificity & sensitivity, procedures to asses QC e.g. levy Jenning charts Cusum plots etc. and rules applied to QC data e.g. Westward's rules. Advantages and disadvantages of various control materials, assessment of various techniques for determining reference ranges and reportable ranges. External quality assessment, proficiency testing programme, identification of sources of analytical and pre analytical errors.

- Fundamentals of total quality management
- Total quality management of the clinical laboratory
- Laboratory error and the six sigma
- Elements of a quality assurance
- Control of Preanalytical variables
- Control of analytical quality using stable control materials and control charts
- Control of analytical quality using patient data
- External quality assessment and proficiency testing programs
- Identifying the sources of analytical errors
- Quality initiatives

COURSES CODE: MB–014

❖ **METABOLISM AND DISEASE (CREDIT HRS 02)**

. This course will review normal metabolic pathways and their regulation and then discuss in depth aberrant metabolism as it contributes to or causes diseases such as diabetes, cancer, and neurodegeneration. Didactic lectures will be complemented with student-based presentations of classic and current primary literature studies.

COURSE CODE: ASC – 010

❖ **RESEARCH METHODOLOGY (CREDIT HRS 01)**

- **Thesis Writing**
  - Literature searching
  - Writing a research proposal
  - Submitting proposals for ethical approval
  - Reporting the results of clinical research
  - Thesis writing
  - Evaluating research reports
  - Sources of funding
- **Foundation of clinical research**
  - Introduction: A Concept of Research
  - The role of theory in clinical research
  - Ethical issue in clinical research

COURSE CODE: ASC – 011

DATA INTERPRETATION (CREDIT HRS 01)

- **Concept of Measurement**
  - Principal of measurement
  - Reliability / validity of measurement
- **Designing Clinical Research**
  - The research question
  - Sampling
  - Experimental control
  - Experimental design
  - Sequential clinical design
  - Single-Case Experimental design
  - Description research
  - Surveys
  - Epidemiology
  - Other research approaches

COURSE CODE: ASC – 012

❖ **BIO STATISTICS (CREDIT HRS 01)**

- **Data Analysis**
  - Description statistics and measures of variability
  - Data management
  - Comparison of group means: The t-Test
  - The analysis of variance
  - Multiple compression tests
  - Nonparametric tests of significance
  - Correlation / Regression
  - Analysis of frequencies chi square
  - Statistics measures of reliability
  - Multiple analysis

COURSE CODE: ASC – 013

- **SPSS-Medical Statistics (CREDIT HRS 01)**
  - Introduction to SPSS
  - Data management
  - Comparison of group means: The t-Test
  - The analysis of variance
  - Multiple compression tests
  - Nonparametric tests of significance
  - Analysis of frequencies chi square
  - Correlation and regression

COURSE CODE: CHP – 014

- **ANIMAL HANDLING (CREDIT HRS 02)**

COURSE CODE: MB-020

- **ADVANCED TOPICS IN MOLECULAR BIOLOGY & CELLULAR SIGNALLING (CREDIT HRS 02)**

  - Landmark developments in genetics and molecular diagnostics
  - Nucleic acid isolation
  - The human genome project
  - Next Generation sequencing

- **Nucleic Acid techniques**

  - Genomes and nucleic acid alteration/mutations/polymorphism
  - Nucleic acid enzymes
  - Advanced Amplification techniques
  - Advanced Detection techniques
  - Advanced Discrimination techniques
  - PCR

COURSE CODE: MB-021

MEDICAL GENETICS AND PAEDIATRIC CLINICAL CHEMISTRY (Credit Hrs 02)

- General principles inheritance, diseases due to inborn errors of metabolism, disorder of amino acid metabolism, disorders of carbohydrate & lipid metabolism, disorder of transport mechanism and storage defects, with special emphasis on clinical importance, diagnosis and screening inborn errors of metabolism and neonatal screening,, techniques for detection of inborn errors of metabolism

  - Provision of service e.g. sample collection, appropriate instrumentation, range of tests etc.
  - Biochemical problems of the newborn e.g. jaundice, hypoglycemia, calcium, phosphate etc.
  - Endocrine problems of childhood e.g. growth, thyroid, adrenal
  - Metabolic problems of childhood e.g. Hypoglycemia, hypocalcaemia,

hyperammonemia.

- Malignancies e.g. neuroblastoma, hepatoblastoma, teratoma, diagnosis and drug monitoring
- Inherited metabolic disorders
- Case discussions / ward rounds
- Implications of modes of inheritance for genetic counseling and antenatal diagnosis
- Molecular pathology of single gene disorders, e.g. familial hypercholesterolemia
- Possible defects in protein biosynthesis arising from genetic mutation; quantitative and qualitative enzyme abnormalities occurring in genetic disorders; the biochemical consequences of a primary enzyme block in a metabolic pathway and the way in which clinical and pathological signs may be produced
- Methods of detecting metabolic disorders with particular consideration to screening selected clinical groups; evaluation of detection programmes; prenatal diagnosis
- Methods of treatment, particularly by dietary restriction and vitamin supplementation, biochemical monitoring of treatment
- Amino acid disorders especially those involving phenylalanine, tyrosine, methionine and homocystine metabolism; the transport disorders, cystinuria and Hartnup disease
- Glycogen storage diseases, galactosaemia, hereditary fructose intolerance
- Organic acidaemias
- Red cell enzyme defects
- Mucopolysaccharide disorders
- Cystic fibrosis

COURSE CODE: CHP– 021

❖ **TOXICOLOGY AND THERAPEUTIC DRUG MONITORING (CREDIT HRS 02)**

- **Clinical Toxicology**
  - Basic Pharmacology of drugs
  - Screening Procedures for Detection of drugs
  - Analysis of Specific drugs and Toxic agents
  - Overdosage with salicylates, barbiturates, paracetamol, tri-cyclic antidepressants, benzodiazepines
  - Accidental poisoning with lead, mercury, carbon monoxide, paraquat and organophosphorus compounds
  - The laboratory investigation of the unconscious patient
  - Drugs of Abuse
  - Effects of ethanol and methanol
- **Therapeutic Drug Monitoring**
  - Pharmaco-Kinetics, and drug dose prediction
  - Sampling for TDM
  - Clinical application of TDM
  - Monitoring of drug therapy. Digoxin and other cardioactive drugs, antiasthmatics
  - Monitoring of Antipsychotic drugs; lithium; I
  - Monitoring of anticonvulsants /antiepileptic drugs
  - Immunosuppressant; cyclosporine, antibiotics
- **Toxic Metal**
  - Basic concept of metal toxicity
  - Diagnosis of metal toxicity
  - Specific heavy metals

COURSE CODE: CHP – 022

❖ **ADVANCED ANALYTICAL TECHNIQUES (CREDIT HRS 02)**

- Understand the principles of laboratory robotics and automation strategies.
- Understand the general principles of assay calibration, QC, and the need

for calibration verification.

- Understand the causes of both positive and negative interferences as well as how to detect and avoid them.
- Understand the techniques employed for specific extraction of analytes from biological fluids.
- Identify factors influencing separation and resolution in electrophoresis and chromatography, including mechanism of separation and mobile/stationary phases.
- For chromatography, understand the importance of internal standards, the relative retention time, carryover, and matrix effects.
- **Selection and analytical evaluation of methods with statistical techniques**
    - Methods section
    - Basic concepts in relation to analytical
    - Analytical goals
    - Method comparison
    - Monitoring serial results
- **Clinical evaluation of methods**
    - Spectrum
    - Classification bias
    - Sensitivity and specificity
    - interpreting a test
    - Cost effectiveness and outcomes research
- **Establishment and use of reference values**
    - The concept of reference values
    - selection of reference individuals
    - Specimen collection
    - Analytical procedures and quality
    - statistical treatment of reference
    - presentation of an observed values in relation to reference values
    - additional topics
- **Preanalytical variables and biological variation**
    - Preanalytical variables

- Biological variability

- **Clinical laboratory information**
  - Computing fundamentals
  - Laboratory information system
  - Pathology informatics resources

COURSE CODE:MB-023 (LAB-II)

ADVANCED MOLECULAR BIOLOGY TECHNIQUES (Credit hr 01)

- DNA extraction
- DNA amplification techniques
- DNA detection techniques
- DNA sequencing
- Next Generation Sequencing
- Techniques in Proteomics

Techniques in Metabolomics

COURSE CODE: CHP – 023

❖ **ADVANCED BIOCHEMICAL ASSAY METHODS LAB-II (CREDIT HRS 01)**

- **Chromatographic Techniques**
  - TLC
  - Sample preparation methods/Desalting
  - Liquid extraction
  - SPE solid phase extraction
  - Column selection and cleaning for HPLC
- **HPLC techniques**
  - HPLC programming/Assay/calculation and interpretation
  - GC programming/Assay/calculation and interpretation
  - GCMS programming/Assay/calculation and interpretation
- **Drugs analysis**
  - Therapeutic drug monitoring

- Screening procedures for drugs
- Drugs and abuse assay
- Ethanol and methanol estimation
- Analysis of specific drug and toxic

- **Atomic absorption spectroscopy/metal analysis**
  - Specific heavy metals assay
- **Electrophoretic Techniques** (Proteins, lipoproteins, Isoenzymes
  - Cellulose acetate
  - Agarose gel
  - PAGE using SDS and gradient gel

COURSE CODE: MB–024

CURRENT ADVANCES IN MOLECULAR BIOLOGY AND MOLECULAR DIAGNOSTICS (CREDIT HRS 02)

- Landmark developments in genetics and molecular diagnostics
- The molecular basis to human genetic diseases
- The molecular basis to infectious diseases
- Molecular diagnostic technologies in healthcare
- Bioinformatics and statistics in molecular genetics
- Research skills in molecular genetics
- Gene annotation

COURSE CODE: CHP – 024

❖ **LABORATORY MANAGEMENT & QUALITY ASSURANCE (CREDIT HRS 02)**

- **Statistical Procedures**

o Standard deviation and error, mode, median and mean

o Reference values and population statistics; analytical goals

o Parametric and non-parametric studies

o Probability statistics; Concept of significance, related statistics

o Linear regression statistics

o The predictive value model, test specificity and sensitivity; receiver operating characteristic curves; likelihood ratios

o Curve fitting routines, handling data from immunoassay techniques

- **Lab Information System**

o Fundamentals of computers; major application area of laboratory computers

o System design and implementation

o Management statistics from laboratory computers

❖ **Laboratory Information System Concepts**

o Understand the major features of a laboratory information system.

o Know the basic data elements of a laboratory information system.

o Demonstrate an awareness of the enterprise information system architecture and how the laboratory information system fits within it.

o Be able to extract data from the laboratory information system

- **Quality Management**

o Fundamentals of total quality management

o A total quality management framework for managing the quality of laboratory tests

o Specimen collection and processing; Sources of biological variation

o Control of pre analytical variables: Dissecting the laboratory system into multiple discrete processes

o Procedures for monitoring pre analytical variables

o control of analytical variables

o Control of analytical quality using stable control materials

- Control analytical quality using patient data

COURSE CODE: CHP-025

❖ **LITERATURE SEARCH, ADVANCED BIOSTATISCS, ADVANCED RESEARCH METHODOLOGY AND MEDICAL WRITING (CREDIT HRS: 2)**

- **Basic Computer Skills**

- Understand terms and concepts related to computer hardware and software.
- Understand basic computer networking concepts.
- Understand how to use word processing, spreadsheet, presentation graphics, and statistical software.

ADVANCED BIOSTATISTICS AND RESEARCH METHODOLOGY

- Analysis of the paired data
- Analysis of variance (ANOVA)
- Randomization and randomization- based analysis
- Survival Analysis
- STROBE and CONSORT

- **The Internet and World Wide Web**

- Know internet-related terms and concepts.
- Be able to utilize the internet to o Access internet-based databases; o Perform literature searches.
- Develop a basic understanding of telepathology systems and concepts.
- Develop a basic understanding of bioinformatics concepts with an emphasis on the critical evaluation of evolving bioinformatics tools. Develop a basic under standing of evolving multiparameter diagnostic spreadsheet,

COURSE CODE: CHP – 026

❖ **CHEMICAL PATHOLOGY – SEMINARS (CREDIT HRS 02)**

Seminars, journal clubs, subspecialty conferences, and participation in multidisciplinary conferences are all useful exercises. Because project management in the development and implementation of laboratory assays is an integral part of the clinical activities of a laboratory medicine physician, it is recommended that each trainee be actively involved in these activities during his/her CP rotations. The experience should be meaningful and substantive and involve the trainee in all aspects of project management and research, including conception, design, execution, analysis, and communication. The process per se is a more

important aspect of the training than the exact target of inquiry. As such, fewer, more involved experiences are preferred. Each student will present the papers from current journals; discussion rather reporting will be emphasized. Students will learn to present and discuss the results of scientific paper. The student will also describe and defend their work in general seminar.

- The candidates after qualifying exam at the end of 1st year who have converted to PhD undergo 18 credit hours of advanced PhD course work. The details of the course work are as under:-

COURSE CODE: CHP – 030

RESEARCH – II (Ph D) (CREDIT HRS 30)

Study for the degree of Doctor of Philosophy involves a sustained, rigorous and systematic approach to the relevant body of knowledge, undertaken through experimentation, archival work, or other appropriate means. It includes an original research project that makes a significant contribution to knowledge and understanding or application of knowledge. It requires the preparation of a substantial thesis that presents the outcome of the research and places it in the broader framework of the discipline or field of study. Undertaken under qualified supervision, it promotes intellectual independence and the capacity to undertake further research at an advanced level. The thesis must meet recognized international standards for such work.

EXAMINATION

For Medical Graduates:

Written Exam: Student will appear in one mid-semester and one end semester exam for each semester. At the end of 1st year the student will appear in comprehensive written exam to be conducted by internal examiner appointed by the RMU Rawalpindi. Those who score >70% in the year 1 comprehensive exam will then take 18 credit hours of advanced PhD course work and appear in two mid-semester and two end semester exams and a comprehensive exam at the end of second year.

Six monthly progress report will be submitted to the university.

For MPhil/FCPS Qualified Candidates: They will take 18 credit hours of advanced PhD course work and appear in two mid-semester and two end semester exams and a comprehensive exam (summative assessment) at the end of second year.

Six monthly progress report will be submitted to the university.

Final Ph.D. Exam

Final PhD Defense of thesis exam will be held at the end of 4 years for MBBS and 3 years for M. Phil/FCPS qualified candidates. This exam will be conducted as per regulation for PhD defense of thesis specified by HEC.

The PhD dissertation will be evaluated by at least two external experts who may be either (i) Pakistan-based Distinguished National Professors, Meritorious Professors, or Tenure Track Professors, or (ii) PhD experts from academically advanced countries (approved list of academically advanced countries for evaluation of PhD Dissertation is provided in Annex 4.4(b) of HEC guidelines for PhD); *provided, however,* that if the PhD candidate publishes his or her dissertation research in a peer reviewed journal that is classified by the HEC as category X or above, the PhD dissertation will only require evaluation by one external expert.

Each PhD researcher shall be required to publish at least one research paper as its first author during his or her doctoral studies in an HEC approved Y category journal (or above) and present 1x research paper in a national conference for the award of PhD degree.

RECOMMENDED BOOKS AND JOURNALS

- Tietz Textbook of Clinical Chemistry and Molecular Diagnostics Burtis CA, Ashwood EA, Bruns DE, eds., 4th ed. St. Louis, MO: Saunders, 2006.
- Clinical Chemistry: Theory, Analysis, Correlation, 4th ed. Kaplan LA, Pesce A, Kazmierczak S, eds St. Louis, MO: Mosby, 2003.
- Clinical Chemistry: Laboratory Management and clinical correlations. SKent Lewandrowskieds. New York. Lippincott Williama & Wilkins.2005.
- William J Marshall and Stephen K Bangert Fifth Edition. Clinical Chemistry 2004.
- National Academy of Clinical Biochemistry. NACB Laboratory Practice Guidelines. http://www.nacb.org/lmpg/main.stm.
- Annals of Clinical Chemistry
- Clinical chemistry and Molecular genetics
- Journal of Endocrinology and Metabolism.