

UNIVERSITY OF CAPE TOWN



ACADEMIC PROGRAMME FOR SPECIALTY TRAINING IN CHEMICAL PATHOLOGY

(2010)

Objectives

This training programme aims to produce good quality Chemical Pathologists, capable of managing clinical laboratories and of contributing effectively to patient care.

Trainees will be expected to have a comprehensive knowledge of, and skills in:

- Basic Sciences and Clinical Chemistry
 - Biochemistry, physiology, and pathology
 - The biochemical and metabolic basis of disease
 - The application of laboratory test results to the investigation and management of patients
 - The provision of specialist opinion in Chemical Pathology
- Laboratory Techniques and Management
 - Physical and chemical principles of analytical techniques and analytical methods
 - The investigation of laboratory problems
 - Accreditation - theory and practice
 - Laboratory administration and management skills
 - Data Management and computational skills
 - Health and Safety requirements for laboratories
- Research
 - Literature review
 - Scientific writing
 - Research methodology

Stages of training

The duration of the training program is five years, comprising two stages of training.

Training occurs at Groote Schuur and Red Cross Children's Hospitals, both tertiary hospitals.

Registrars are encouraged to attend relevant clinics throughout the duration of the training program, particularly paediatric and adult endocrinology and lipidology clinics.

Registrars rotate through the various laboratory sections as described in the Registrar Training Manual. Structured visits to outside laboratories are included in the training, which include, but are not limited to, the porphyria laboratory and pharmacology.

Registrars will be taught to authorise work within the first few months of training and will thereby be exposed to a large variety of different clinical cases, while simultaneously obtaining skills and experience in laboratory medicine.

Part I

a. Induction period

This is a six week induction period where registrars will be introduced to the various areas in the laboratory, as well as be exposed to laboratory techniques and basic chemical pathology.

They will be expected to complete and submit sections A and B in the Registrar Training Manual by the end of the induction period.

Registrars will be trained in the use of the laboratory information system. They will also receive training in the validation and monitoring of clinical results and will be expected to be competent in this function by the end of the induction period.

b. Primary training

This is an 18 month period of time during which registrars will receive tutorials and laboratory training so as to provide competence in the following areas:

- Biochemistry and the metabolic basis of disease
- Knowledge of the pathophysiology of disease
- Basic knowledge of Chemical Pathology
- Principles of laboratory techniques, methods and instrumentation, including molecular biology
- Quality control and proficiency testing
- Basic laboratory management
- Literature review and at least one research output

The following will be examinable by the end of the first 18 months in the form of the Part I exam (discussed later) (recommended literature included):

Section 1: Basic Applied Chemical pathology

This consists of a basic chemical pathology primer at the level of the old curricula taught to medical students

Books

- Clinical Chemistry, Willaim J Marshall, Stephen K Bangert
- Chemical pathology lecture notes from the Division of Chemical Pathology, University of Cape Town
- Contemporary Practice in Clinical Chemistry, Clarke W and Dufour DR, AACC Press 2006. Chapters 17 – 42.

Section 2: Biochemistry

This consists of fundamental medical biochemistry as taught generally at BSc 2nd year level and includes all the biochemical pathways of intermediary metabolism, molecular biochemistry as well as special applied biochemistry such as the biochemistry of certain proteins (eg haemoglobin and immunoglobulins) and special biochemical pathways (bilirubin metabolism, purine metabolism,

haem biosynthesis and steroid synthesis) and pathways typically involved in metabolic disease (glycogen synthesis and lysis, urea cycle, fat oxidation, branch chain amino acid oxidation etc).

Books

- Lippincott's Illustrated Reviews: Biochemistry, Pamela C Champe, Richard A Harvey
- Metabolism At a Glance, Jack Salway

Section 3: Applied physiology

This consists of those areas of human physiology that are particularly pertinent to the practice of chemical pathology.

Books

- Review of Medical Physiology, Ganong

Section 4: Endocrinology

This consists of a detailed understanding of Endocrinology and associated endocrinological diseases and the pathophysiology thereof.

Books

- Greenspan's Basic & Clinical Endocrinology, Gardner et al, Lange (Publisher).

Section 5: Medical Statistics

This consists of a fundamental primer in medical statistics at the level of the recommended textbook

Books

- Medical statistics at a glance, Aviva Petrie

Section 6: Molecular genetics

This consists of a fundamental primer in human genetics and epigenetics and covers the principles of molecular laboratory analysis at the level of the recommended textbook

Books

- Medical genetics at a glance, Dorian J Prichard

Section 7: Analytical Techniques and Instrumentation

This consists of in depth study and understanding of the fundamental principles behind all routine and specialized methods used to analyze compounds relative to the practice of Chemical Pathology at the level covered by the recommended textbook. The emphasis here is in understanding the principles of analytical methods as opposed to the details of specific methods for specific analytes.

Books

- Clinical Chemistry: Theory, Analysis, Correlation, Kaplan & Pesce
- Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Carl A Burtis – chapters 1-10 and 37

Section 8: Basic Laboratory Skills

Basic laboratory skills at the level of a Part 1 candidate should be equivalent to any technologist who performs routine chemistry and molecular manual and automated assays and the student should be able to follow any routine bench manual Standard Operating Procedure used in any laboratory in South Africa, given access to the required reagents and instrumentation. Training

facilities for this purpose are be available within the routine training laboratory and these skills will be examined in a Part 1 wet practical exam.

Formal assessment is performed by means of a University of Cape Town MMed Part I exam which includes written, practical and oral exam. This exam may be taken after 12 months of training, but must be successfully completed within 18 months.

NB. Registrars will be expected to have completed and submitted the Registrar Training Manual Exercises before being allowed to sit for the MMed Part I exam.

Part II

Registrars continue to rotate through the different laboratory sections with the aim of increasing the depth of their knowledge and understanding of clinical and laboratory principles. They will also be expected to obtain this deeper understanding through self-study (using the curriculum and recommended texts listed below) and through keeping abreast of relevant literature (journals listed below).

Registrars will consult with clinicians regarding difficult clinical cases and laboratory staff regarding technical issues. In this way, they will develop trouble shooting skills. Furthermore, they will participate in laboratory management.

Formal assessment is performed by means of South African College of Medicine FC Path. These exams will comprise written, practical and oral components.

Registrars will be expected to submit their completed MMed Mini Dissertation before being allowed to sit the Part II exam.

Part III (Mini Dissertation)

This comprises the research component of the training program and consists of the preparation and execution of a research project.

Students are expected to:

- Write a research proposal
- Literature review
- Apply for ethics clearance
- Apply for Departmental Research Council approval
- Draw up a research budget
- Apply for research funding, if required
- Data collection
- Data analysis
- Write of findings as mini thesis and submission for marking by external examiners as per the university protocol
- Publication in a peer-reviewed journal will be encouraged

- This written dissertation must comply with the University recommendations – Appendix attached.

This research project will be identified after completion of Part I and must be submitted before the Part II exam can be written.

Training requirements

a. Rotations and clinics

Registrars will participate in the following ward rounds: Combined Endocrinology ward round, Medicine grand ward round and lipidology ward round.

Registrars will be required to attend clinics particularly endocrinology, paediatrics endocrinology and lipidology clinics.

Communication with clinicians is encouraged.

Registrars will rotate through different sections of the C17 chemical pathology laboratory, the porphyria laboratory (1 week), the molecular medicine laboratory (1 month) and the Red Cross Children's Hospital (3 months). Registrars will also be encouraged to visit external laboratories in order to gain experience with analysers / analytical techniques not available at the training sites.

b. Practical laboratory work

Registrars will receive practical experience in laboratory testing and laboratory management (under supervision). They should have an understanding of how a modern laboratory service is organized, how different staff groups contribute to the pre-, intra- and post-analytical processes and how the service operates within the hospital and the health service. Registrars are expected to gain hands-on experience and be able to perform all manual and specialist assays in the laboratory.

c. Teaching

Registrars will be required to participate in undergraduate teaching of the MBChB students and laboratory staff.

d. Presentations

Registrars are required to attend and present talks at the following meetings:

- Medicine Grand Ward Round
- Endocrinology Seminar
- Chemical Pathology Journal Club
- Conferences / Symposia / CME Meetings

e. Log book

All registrars will be issued with a logbook in which all test procedures performed, case presentations, seminars/ talks presented, clinics attended, tutorials / lectures attended should be recorded and signed by the relevant consultant / scientist / senior technologist. This will constitute a training record. This book will form part of the registrar evaluation process.

f. Weekly timetable

- Monday: Chemical Pathology Journal Club
- Tuesday: Endocrinology Seminar; Lipidology ward round
- Wednesday: Lipidology tutorial; Journal discussion tutorial
- Thursday: Biochemistry tutorial; Medicine grand round
- Friday: Management tutorial; Endocrinology ward round

g. Recommended reading

Text books

Biochemistry & Physiology

- Lippincott's Illustrated Reviews: Biochemistry, Champe PC et al, Lippincott Williams & Wilkins.
- Metabolism at a glance, Salway et al
- Review of Medical Physiology, Ganong

Statistics & calculations

- Medical statistics at a glance, Petrie and Sabin
- Calculations in Laboratory science by Allan Deacon Published by Ace Venture Puplications 2009
- Deacon's Challenge –ACB News - Association for Clinical Biochemistry

General

- Greenspan's Basic and Clinical Endocrinology. Greenspan FS, Forsham PH (Eds.), David Gardener 8th ed. Lange Series. Appleton and Lange, 2007.

Molecular Genetics

- Medical genetics at a glance, Dorian J Prichard

Clinical Chemistry

- Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, Burtis, Ashwood, Bruns. 4th Ed, 2006
- Clinical Chemistry. Theory, Analysis and Correlation. Kaplan LA, Pesce AJ. 5th Ed. Mosby, 2009.
- Contemporary Practice in Clinical Chemistry, Clarke W, Dufour DR (AACC)
- Clinical Chemistry, 4th edition, Marshall WJ (Mosby)

Journals

- American Journal of Clinical Pathology.
- Journal of Clinical Pathology
- Annals of Clinical Biochemistry
- New England Journal of Medicine
- Clinical Chemistry
- Clinical Biochemistry Reviews
- Clinics in Laboratory Medicine
- Clinica Chimica Acta
- Scandinavian Journal of Clinical and Laboratory Investigation Science
- Journal of Clinical Investigation
- Nature Medicine

- Nature Genetics
- Nature
- Science
- Cell

Assessments and examinations

Registrars will be formally assessed at 6 monthly intervals, by oral and/or written (3 hours) and practical (3 hours plus OSCE) examination.

Six monthly evaluation meetings will take place to discuss current progress and any issues / feedback that the registrar / consultants may have regarding his training.

Formal examinations:

For Part I and Part II, as described under Stages of training.

Furthermore, on-going assessment will include the following:

- Each registrar is required to complete at least 1 output per year (an output is a written submission of either a case presentation, an audit or an operational or research investigation, written in the form of a publication– publications in peer reviewed journals are encouraged)
- The logbook content will be assessed at the six monthly evaluation meetings
- Registrar presentations at the various forums
- Routine work will be evaluated by consultants in conjunction with senior laboratory personnel

Detailed Curriculum

Laboratory Principles

- Water – purification, storage, handling and grading of water
- Chemicals – grading and storage; reference materials
- Units of measurement
- Handling of glassware and laboratory equipment
- Centrifugation
- Gravimetry
- Thermometry
- Volumetry
- Buffer Solutions
- Calculations in clinical chemistry
- Specimen collection and processing

Laboratory Techniques

- Pre- and post- analytical variation
- Spectral techniques (principles, instrumentation and limitations)
 1. Absorption spectroscopy
 2. Atomic absorption
 3. Flame photometry

4. Fluorometry
 5. Nephelometry and turbidimetry
 6. Refractivity
 7. Reflectance photometry
 8. Chemiluminescence
 9. Phosphorescence
- Chromatography
 1. Basic concepts
 2. Resolution
 - Theoretical plates and efficiency
 - Retention
 - Selectivity
 3. Planar chromatography
 4. Column chromatography
 5. Ion-exchange
 6. Partition
 7. Adsorption
 8. Affinity
 9. Size-exclusion
 - Mass Spectrometry
 1. Basic concepts
 2. Ion sources
 3. Vacuum systems
 4. Mass analysers
 5. Detectors
 6. Separation techniques
 - LCMS
 - GCMS
 7. Tandem MS
 8. MALDI-TOF
 9. SELDI-TOF
 10. ICP MS
 11. Clinical applications
 - Immunoassays
 1. Basic concepts
 - Antigen-antibody reactions
 - Cross-reactivity
 - Scatchard analysis
 - Competitive immunoassays
 - Non-competitive immunoassays
 - Homogeneous and heterogeneous immunoassays
 - Mechanisms of interference
 - Specificity and sensitivity
 2. Qualitative methods
 - Precipitation techniques
 - Western blotting

- 3. Quantitative methods
 - Turbidimetry and nephelometry
 - Indicator-labeled immunoassays
 - Radioimmunoassays
 - Enzyme linked immunoassays
 - Chemi- and electrochemiluminescence
 - Fluorescent polarization immunoassays
- Electrophoresis
 1. Basic concepts and theory
 - Electrolytes, isoelectric points and electric fields
 - Electro-osmosis
 - Support media
 - Isoelectric focusing
 2. Gel electrophoresis
 - Protein, DNA and lipids
 - Support media
 - Buffers and stains
 3. Capillary electrophoresis
 - Capillary zone electrophoresis
 - Capillary gel electrophoresis
 - Capillary iso-electric focusing electrophoresis
 - Capillary isotachopheresis
 4. Microchip electrophoresis
 5. Immunofixation and immunosubtraction
- Electrochemistry
 1. Basic concepts
 - Potentiometry
 - Voltammetry / Amperometry
 - Conductometry
 - Coulometry
 - Ion selective electrodes
 2. Optical chemical sensors
 3. Biosensors
 4. In vivo and minimally invasive sensors
 5. Clinical applications
 - Gas sensing electrode
 - pH electrode
 - Glucose electrode
 - Potassium electrode
 - Sodium electrode
 - Chloride electrode
 - Ammonia electrode
 - Lithium electrode
- Enzymology
 1. Basic principles

- Isoenzymes and isoforms
 - End-point and kinetic assays
 - Enzyme kinetics
- 2. Analytical enzymology
 - Applications
 - Standardization
 - Mass and activity assays
- Measurement of colligative properties
 1. Basic concepts
 - Principles of measurement
 - Osmolality and osmolarity
 - Clinical osmometry
- Interferences in chemical analysis
 1. In vitro interferences
 2. In vivo interferences
 3. Evaluation of analytical interference
- Molecular diagnostics
 1. Basic concepts
 - Structure of DNA and RNA
 - Replication, transcription and translation
 - Mutations and gene expression
 - Inherited diseases
 2. Techniques of DNA analysis
 - Amplification techniques
 - PCR and RT-PCR
 - Qualitative and quantitative
 - Other forms of amplification
 - Techniques for mutation analysis
 - Electrophoresis techniques
 - Restriction enzyme digestion and gel electrophoresis
 - Southern transfer
 - Heteroduplex migration analysis
 - Single-strand conformation polymorphism analysis
 - Denaturing gradient gel electrophoresis
 - Temperature gradient electrophoresis
 - DNA sequences techniques
 - Capillary electrophoresis
 - Single nucleotide extension
 - Pyrosequencing
 - Mass spectrometry
 - HPLC
 - Hybridisation assays
 - Melting analysis
 3. Design of molecular diagnostics laboratory
 4. Pharmacogenetics and pharmacogenomics

Laboratory management

- Evidence based laboratory medicine
- Clinical audit
- Traceability and measurement uncertainty
- Quality management
 1. External quality assurance
 2. Internal quality control
 3. Quality control charts
 4. Westgard rules
 5. Six sigma
- Laboratory informatics
- Statistics
 1. Population distributions
 - Measures of central tendencies
 - Measures of variation
 - Confidence intervals
 - Accuracy and precision
 2. Parametric and non-parametric tests
 3. Regression and correlation
 4. Sensitivity
 5. Specificity
 6. Predictive values
 7. Odds ratios and likelihood ratios
 8. Bayesian analysis
 9. Receiver operating characteristic curves
- Accreditation
 1. Different types of audit
 2. SANAS; CAP and other accreditation bodies
 3. ISO 15189
- Reference Intervals
 1. Establishment of reference intervals
 - Non-parametric
 - Parametric
 2. Transferability of reference intervals
 3. Multivariate reference regions
 4. Clinical decision limits
- Biological variation
 1. Monitoring serial results
 2. Reference change values
 3. Delta check
 4. Index of individuality
 5. Allowable error limits
- Automation
 1. Concepts of automation
 - Test repertoire
 - Random access

- Continuous flow
 - Batch analyser
 - Throughput
 - Stat testing
 - Cost
- 2. Laboratory processes
- 3. Automated laboratory systems
- 4. Trouble shooting and training
- 5. Total laboratory automation
- Point of Care Testing (POCT)
 1. Use of near patient testing
 2. Implementation and monitoring of POCT
 3. Quality assurance monitoring
 4. Cost assessment
 5. POCT technology
 6. Data integration and connectivity
- Method evaluation
- Budgets and cost analysis
- Ethics
- Laboratory Safety
 1. General safety practices
 2. Waste and chemical control
 3. Safety equipment
 4. Safety inspections
 5. Ergonomics
 6. Laboratory hazards

Biochemistry and pathophysiology

- Water and electrolytes
 1. Body water compartments
 2. Regulation of body fluid compartment osmolarity and volume
 3. Water metabolism
 4. Sodium metabolism
 5. Potassium metabolism
 6. Chloride metabolism
- Acid base
 1. Acid-base balance
 - Respiratory mechanisms
 - Renal mechanisms
 2. Buffer systems
 3. Acid base disorders
 - Acidosis
 - Alkalosis
 4. Instrumentation
- Lipidology
 1. Basic biochemistry

- Lipids
 - Lipoproteins and apolipoproteins
 - 2. Lipoprotein metabolism
 - 3. Clinical lipidology
 - 4. Measurement of lipids and lipoproteins
- Amino acids and proteins
 1. Basic biochemistry
 2. Plasma proteins
 3. Complement proteins
 4. Immunoglobulins
 5. Clinical implications
 6. Measurement techniques
- Extravascular biological fluids
 1. Serous fluids
 2. Synovial fluids
 3. Cerebrospinal fluid
 4. Saliva
 5. Urine
 6. Stool
- Renal function
 1. Renal physiology
 2. Pathophysiology of renal disease
 3. Renal function tests
- Liver function
 1. Liver physiology and biochemistry
 2. Clinical manifestations of liver disease
 3. Liver function tests
- Bone disease
 1. Biochemistry and physiology of bone
 - Calcium
 - Phosphate
 - Magnesium
 - Hormone regulation
 2. Bone disorders
 3. Markers of bone turnover
- Gastro-intestinal system
 1. Physiology and biochemistry of GIT function
 2. Disorders of the GIT system
 3. Gastrointestinal function tests
- Cardiovascular system
 1. Cardiac physiology
 2. Cardiac disease
 3. Cardiac biomarkers
- Iron and haem metabolism
 1. Iron, haem and bilirubin metabolism
 2. Disorders of iron, haem and bilirubin metabolism

- 3. Iron studies
 - 4. Porphyrins
- Biochemical aspects of haematology
 - 1. Haemoglobin biochemistry
 - Oxygen affinity and transport
 - 2,3-bisphosphoglycerate
 - 2. Haemoglobinopathies and other inherited haemoglobin disorders
 - 3. Thalassaemias
 - 4. Myelodysplastic disorders
 - 5. Acquired haemoglobin disorders
 - Methaemoglobinaemia
 - Carboxyhaemoglobin
 - Cyanohaemoglobinaemia
 - 6. Analytical methodology
- Vitamins and trace elements
 - 1. Biochemistry
 - 2. Water soluble vitamins
 - 3. Fat soluble vitamins
 - 4. Trace elements
 - 5. Analytical methodology
- Nervous system
 - 1. Physiology and biochemistry
 - Blood brain barrier
 - Composition and function of cerebrospinal fluid
 - 2. Neurological disease
 - 3. Cerebrospinal fluid testing
- Tumour markers
 - 1. Pathophysiology of cancer
 - 2. Tumour biomarkers
 - Screening
 - Monitoring
 - Staging
- Toxicology
 - 1. Pathophysiology of toxins
 - 2. The toxicology laboratory
 - Analytical methodology
 - Screening
 - Monitoring
- Therapeutic drug monitoring
 - 1. Basic concepts
 - Mechanism of action
 - Pharmacokinetics
 - 2. Specific drug groups
 - 3. Clinical applications
 - 4. Analytical methodology
- Endocrinology

1. General
 - Chemical nature of hormones
 - Mechanisms of hormone action
 - Regulation of hormone synthesis and release
2. Hypothalamic and pituitary hormones
 - Disorders of hypothalamus and pituitary
 - Hypothalamic and pituitary function tests
3. Thyroid
 - Thyroid hormone physiology
 - Thyroid dysfunction
 - Tests of thyroid function
4. Gonads
 - Normal ovarian and testicular function
 - Disorders of ovaries and testes
 - Gonadal function tests
 - Infertility
5. Adrenals
 - Adrenal cortex
 - Steroid biochemistry
 - Control, regulation and action of steroid hormones
 - Disorders of the adrenal cortex
 - Adrenal cortex function testing
 - Adrenal medulla
 - Catecholamine biochemistry and physiology
 - Disorders of adrenal medulla
 - Analytical methodology
6. Diabetes mellitus
 - Glucose and insulin metabolism
 - Classification of diabetes mellitus
 - Pathogenesis of diabetes mellitus
 - Complications of diabetes mellitus
 - Tests for diabetes mellitus and its complications
- Nutrition
 1. Nutrient classes
 2. Nutrition in health and disease
 3. Therapeutic nutrition support
 4. Nutrition and inborn errors of metabolism
 5. Biochemical monitoring of nutritional status
- Paediatric clinical biochemistry
- Pregnancy
 1. Physiology of pregnancy
 2. Biochemistry of amniotic fluid
 3. Maternal biochemical changes during pregnancy
 4. Fetal biochemical changes during prenatal development
 5. Pathological conditions associated with pregnancy
 6. Testing and monitoring in pregnancy

- Diagnosis of pregnancy
 - Antenatal screening
 - Fetal lung maturity testing
 - Testing for pregnancy-related diseases
- Inborn errors of metabolism
 1. Biochemistry
 2. Disorders of amino acid metabolism
 3. Disorders of organic acid metabolism
 4. Disorders of fatty acid oxidation
 5. Analytical considerations
- Biochemical aspects of immunology
 1. The immune system
 2. Disorders of the immune system
 - Hypersensitivity
 - Autoimmune disorders
 3. Infection and sepsis

In addition to the contents of the above curriculum, registrars will be exposed to and trained in the following analytical techniques

- HPLC
- Gas chromatography
- Mass spectrometry – including MS/MS, MALDI-TOF MS and ICP-MS
- NMR spectrometry
- Atomic absorption
- Real Time PCR – eg Light Cycler with various probes
- Sequencing PCR
- Capillary electrophoresis
- Manual enzyme assays using fluorometric and radioactive detection and measurement
- Dynamic endocrine function testing and intraoperative endocrine testing
- Measurement of GFR by way of clearance of radioactive tracers as well as other techniques such as inulin and iohexal clearance