

## The IFCC Curriculum - phase 1

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*IFCC Committee for Distance Learning – for the IFCC eAcademy project*

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### IFCC CURRICULUM

#### THE IFCC CURRICULUM - PHASE 1



The IFCC Curriculum was developed as part of the **IFCC eAcademy** project by the Committee for Distance Learning.

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## INTRODUCTION

The IFCC curriculum is being developed as a guide for its member societies in their development of syllabuses for postgraduate trainees in laboratory medicine, appropriate for use in their own countries. The curriculum should be viewed as a framework into which requirements specific to different regional or national practice can be incorporated.

It is also intended to provide a resource for trainees in planning their private study in preparation for academic and professional qualifications which lead to formal recognition of expertise and status as experts and leaders in the field of laboratory medicine.

The curriculum has been developed in response to a request from some National Societies, by the Committee on Distance Learning (C-DL) and will inform the development of the IFCC e-Academy. The C-DL is grateful to the following National Societies who responded to the call in 2013 and submitted their own curricula for us to consult in considering format and content:

- Australia and New Zealand
- Canada
- Croatia
- Netherlands
- Romania
- Slovak Republic
- South Korea
- Sweden
- Switzerland

A laboratory medicine expert is expected to have a comprehensive knowledge of the science and medicine on which the specialty is based and to use this knowledge to develop and provide a safe, effective, efficient and high quality service to its users. The curriculum is designed to provide a framework of learning both practical and theoretical components through which this expertise can be achieved.

Herein, is phase 1 of the IFCC curriculum to support ongoing education in laboratory medicine. It is not intended to include references in this curriculum. Instead, the learning objectives are designed to link back to the online learning material of the IFCC eAcademy where relevant additional reading will be provided within these presentations, Figure 1.

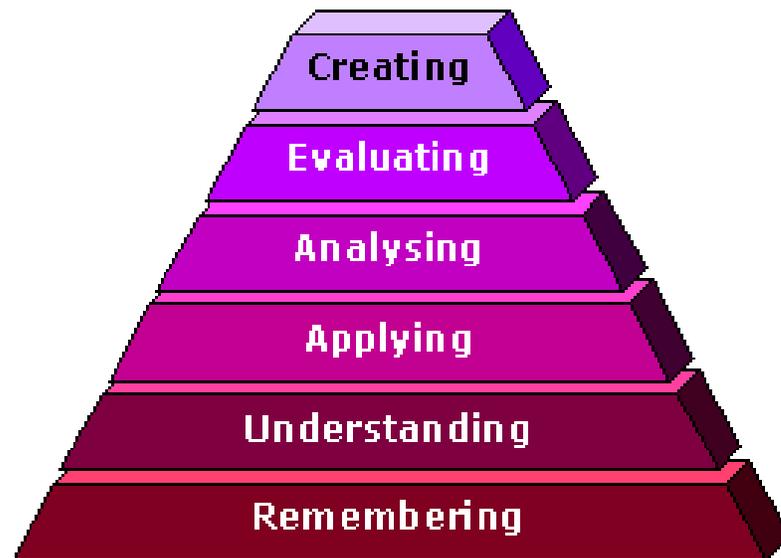
### *Learning Skills*

IFCC recommends a stepwise approach to the acquisition and application of knowledge by trainees. Bloom's taxonomy defines six categories and cognitive processes, refined in 2001<sup>1</sup>. Each category is shown with appropriate verbs that may be used to construct learning objectives or assessment questions.

- **Remembering** - retrieving, recognizing, and recalling relevant knowledge  
*Define, memorise, list, name*

- **Understanding** - constructing meaning through interpreting, exemplifying, classifying, summarizing, inferring, comparing, and explaining  
*Restate, discuss, describe, identify, report, explain, review, recognise*
- **Applying** - carrying out or using a procedure through executing, or implementing  
*Translate, interpret, apply, illustrate, demonstrate, use*
- **Analysing** - breaking information into parts to explore understanding and relationships through differentiating, organizing, and attributing  
*Distinguish, differentiate, appraise, analyse, calculate, compare, contrast*
- **Evaluating** - making judgements based on criteria and standards through checking and critiquing  
*Appraise, evaluate, revise, score, estimate, choose, assess*
- **Creating** - putting elements together to form a coherent or functional whole; generating new ideas, products or ways of viewing things  
*Compose, plan, propose, design, prepare, organise*

**Figure I** In diagrammatic form, the learning process, creating and evaluating are key functions for those in the most senior professional roles.



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<sup>1</sup> Bloom B S (ed.) (1956) Taxonomy of Educational Objectives, the classification of educational goals – Handbook I: Cognitive Domain New York: McKay)

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### **Program Learning Objectives**

Many components contribute to safe and effective laboratory investigation of patients and their diseases. These can be summarised in Figure II.

Figure II Program Learning Objectives - Summarised

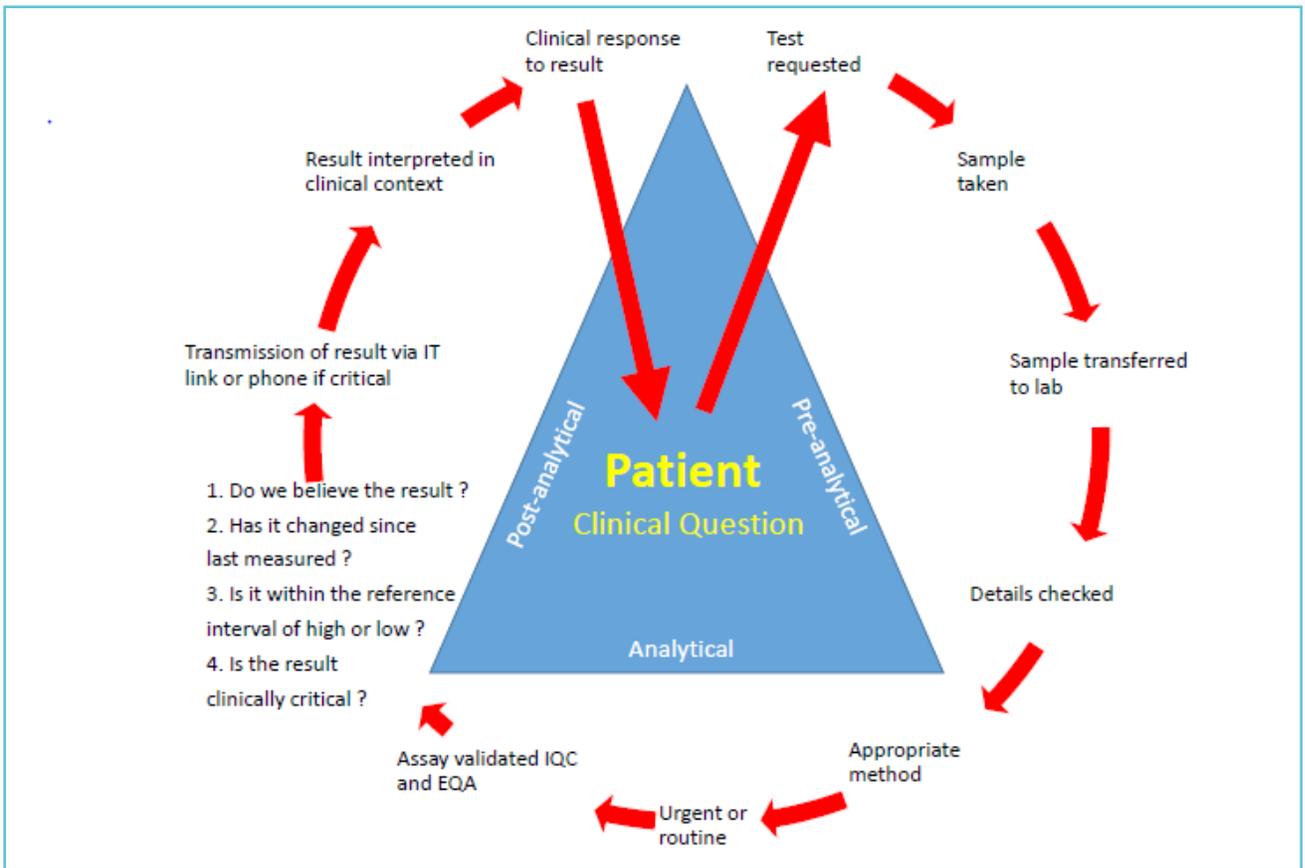


Figure II. The specialist functions of a clinical scientist are:

- To advise on testing protocols and the appropriateness of testing
- To provide meaningful analytical results that can be used with confidence in the diagnosis and management of patients with disease.
- To provide interpretation of laboratory results in the light of clinical findings in the individual patient.
- To reach this level of expertise the clinical scientist must have detailed knowledge of:
  - ◇ Human physiology, biochemistry and organ function
  - ◇ The causes, clinical signs and symptoms of disorders of organs, systems, metabolic disease and genetic disease
  - ◇ Laboratory analyses and testing protocols for investigation of such disorders
  - ◇ The options for and principles of measurement of specific analytes
  - ◇ The pre-analytical, analytical and post analytical factors that may influence testing
  - ◇ The limitations of analyses, including specificity, sensitivity, bias and imprecision
  - ◇ Biological variation, reference intervals and critical test results

### Clinical Interpretation

Clinical interpretation of laboratory results is complex and it is important to adopt a systematic approach. There must be procedures in place in the laboratory, to ensure that specimen quality can be guaranteed and that the analytical quality of the result is fit for purpose. The result can then be interpreted with respect to reference intervals, clinically critical limits or significant changes in value and the causes of any abnormal or unexpected laboratory results be considered. It is very useful to have a structured approach to help interpretation of results, particularly those that are unexpected or unfamiliar. Considering the possible underlying pathological processes is an excellent starting point and using an acronym such as the one shown below, provides structure to the thought processes and minimises the risk of missing an important element.

A useful memory prompt is “A Vitamin C Def” (Table 1).

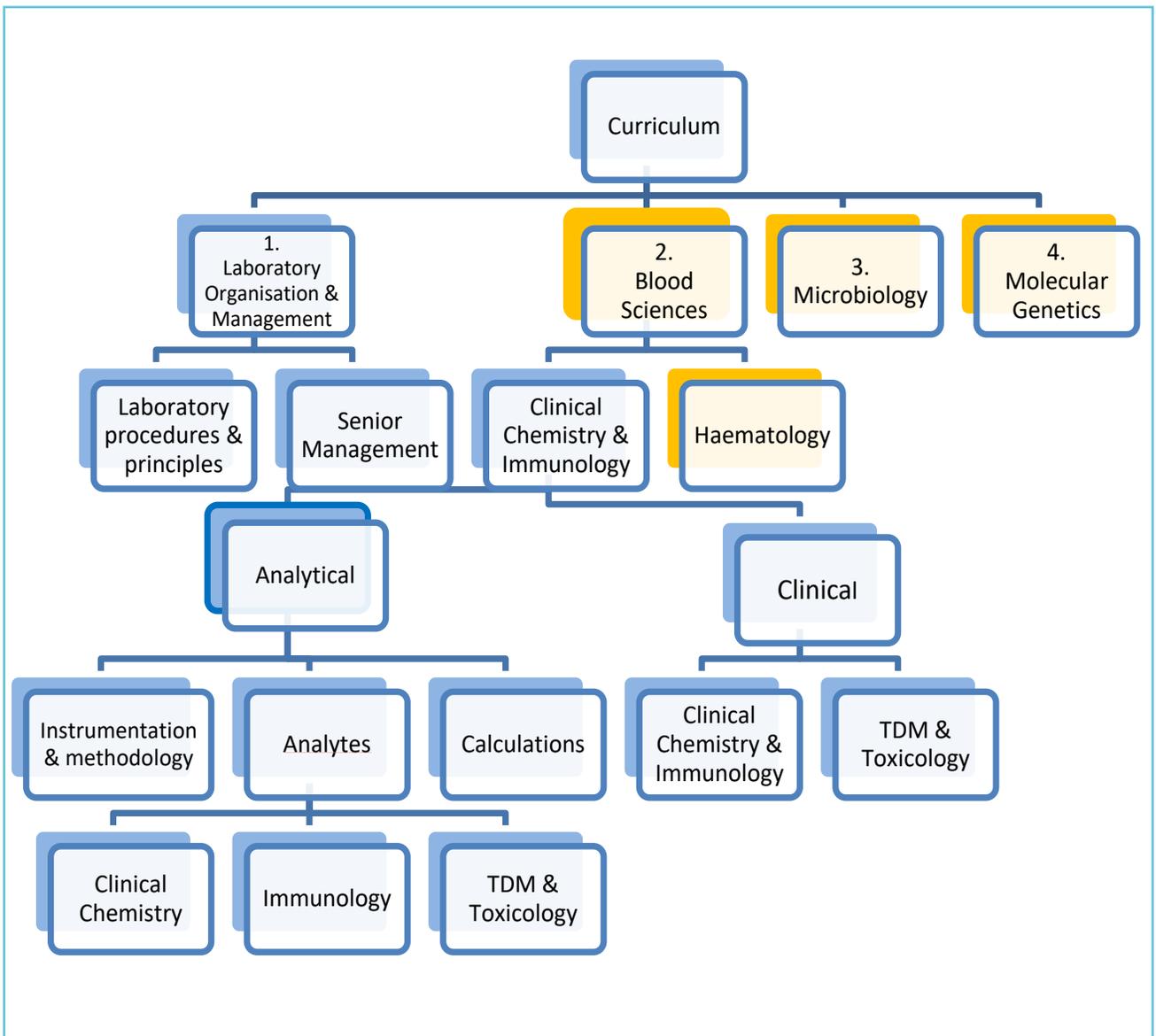
Table 1	A VITAMIN C DEF acronym to use as a memory prompt
A	acquired
V	vascular
I	infective/inflammatory
T	traumatic
A	autoimmune
M	metabolic
I	iatrogenic/idiopathic
N	neoplastic
C	congenital
D	degenerative/developmental
E	endocrine/environmental
F	functional

### Curriculum Structure

The curriculum is designed to represent the three specialties of laboratory medicine; Blood Sciences, Microbiology and Molecular Genetics. Within each of the specialities, clinical and analytical aspects are considered separately and there is further breakdown of the clinical section into sub-specialties. These are then subdivided into disease groupings, based on organ system, metabolic disease and genetic disease. Within each of these groupings, individual clinical conditions are specified. Analytical aspects are broken down primarily into technology groupings then further into specific techniques. The whole structure is therefore presented in a hierarchical way. Laboratory Organisation and Management, common to all specialties, is considered separately.

In this version (i.e. part one) of the curriculum, concepts related to Laboratory Organisation and Management and Blood Sciences (Clinical Chemistry and Immunology) have been developed. Future additions to the curriculum will include curricula related to Haematology, Microbiology, and Molecular Genetics, Figure 3.

**Figure III** Summary of Curriculum Design



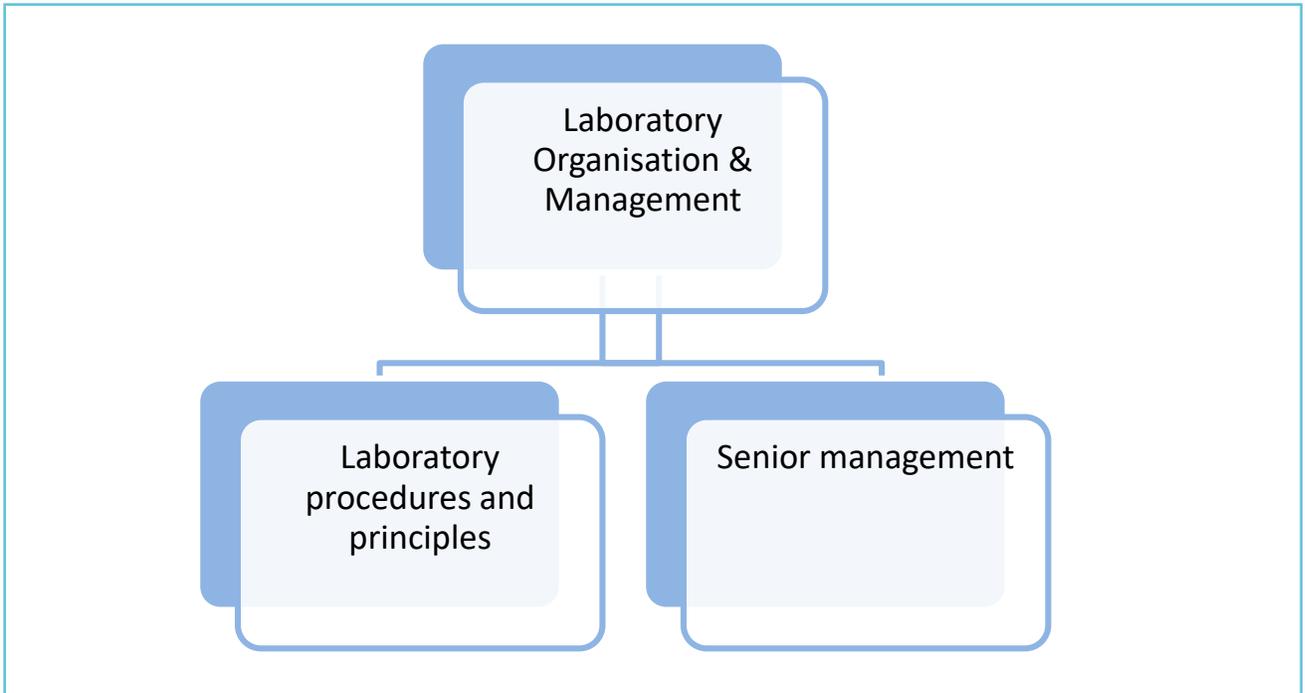
**Figure III:**

- The sections covered in version 1 of the curriculum are shown in blue.
- The yellow cells indicate areas of the curriculum to be developed further as part of future versions.

## SECTION A: LABORATORY ORGANISATION AND MANAGEMENT

Laboratory Organisation and Management skills and concepts are considered in two categories, those which are relevant to all laboratory staff and those which are required by those in senior laboratory roles who have responsibilities for leadership in all aspects of the service.

**Figure A1** Hierarchical structure of Laboratory Organisation and Management section of the curriculum



### **Section A1. Laboratory Principles and Procedures: Learning Objectives**

**Be able to discuss and demonstrate specific skills and competences for laboratory organisation and management**

- Basic information communication technology (ICT) skills
- Basic instrument and equipment maintenance
- Basic research skills
- Basic statistical techniques
- Biological variation
- Document control
- External quality assessment (EQA)
- Health and safety issues
- Internal quality control (IQC)
- Laboratory safety
- Method evaluation
- Patient safety
- Pre-analytical variables
- Reference intervals (RI)
- Specimen collection
- Specimen preparation
- Standard curves
- Standard operating procedures
- Temperature monitoring

- Waste management
- Water purity monitoring

### **Section A2. Senior Laboratory Management: Learning Objectives**

**Be able to discuss and demonstrate specific skills and competences for laboratory organisation and management at a senior or advanced level**

- Accreditation and ISO15189
- Advanced communication skills
- Advanced research skills
- Budget management
- Clinical and professional liaison
- Evidence-based laboratory medicine
- Facilitating training and continuing professional development (CPD) for all department staff
- Initiation of and collaboration in research activities
- Instrumentation and method selection
- Laboratory information systems (LIS), hospital information systems (HIS) and interfaces
- Medico-legal requirement and legislation
- Personnel management
- Point of care testing policies and management
- Professional ethics
- Requesting and reporting policies
- System design
- Total quality management and quality systems
- Traceability

### **Section A3. Evidence Based Laboratory Medicine (EBLM): Learning Objectives**

**Be able to discuss the relevance of evidence based laboratory medicine as applied to your organisation at an advanced level**

#### **Core topics**

- Economic Evaluation of Diagnostic Tests
- Evaluating the literature: Appraisal instruments; e.g. STEP
- Evidence Based Laboratory Medicine (EBLM): definition, how it differs from Evidence Based Medicine (EBM) and why we need it
- The EBLM process: Ask, Acquire, Appraise; Act, Audit
- Formulation of the Question (PICO; CAPO and other formats)
- Guideline development, levels of evidence and appraisal. AGREE instrument
- Laboratory Medicine and Clinical Outcomes; Applying the Evidence
- Meta-analysis
- The Role of Clinical Audit
- Searching the Evidence; PubMed; EMBASE; Cochrane Library
- Sources of bias in studies of diagnostic accuracy, STARD criteria
- Study design: cross-sectional, cohort and randomized controlled trials (RCTs)
- Systematic Reviews versus Narrative Reviews
- Sources of Guidelines. Cochrane Collaboration

#### **EBLM: measures of diagnostic performance**

- Sensitivity, Specificity, Predictive Value, Effect of Prevalence

- Likelihood Ratios (and their utility), Odds Ratios – Fagan’s nomogram
- Receiver Operating Characteristic (ROC) Curve analysis

### ***Evidence Based Laboratory Medicine and Point of Care Testing (POCT)***

- Outcomes of relevance for laboratory tests, including POCT
- Examples of evidence base for POCT including HbA1c, the Emergency Department, self-monitoring of blood glucose and INR testing
- POCT troponin testing and rural health; examples from Australia
- POCT in the Primary Care environment

### ***Section A4. Conducting Research in Laboratory Medicine: Learning Objectives***

**Be able to discuss the key aspects related to the conduct of research in laboratory medicine**

#### ***Why is research in laboratory medicine important?***

- To describe medical research
- To discuss the types of medical research that are undertaken
- To define laboratory medicine in the context of the research guide
- To explain why research in laboratory medicine is important to stakeholder groups

#### ***Choice of suitable project***

- To describe factors that stimulate research projects
- To discuss how the importance of research may be assessed
- To consider the practicability of a research project

- To explain research supervision and mentoring

#### ***Conduct a literature search***

- To describe literature study
- To explain the questions to be asked when reading a research publication
- To recognise the importance of critical appraisal
- To discuss how critical appraisal of research publications is undertaken

#### ***Formulating a research plan***

- To discuss the research question
- To explain the importance of hypothesis based research
- To describe the construction of aims and objectives
- To consider the research design

#### ***Submitting a research proposal for external approval and funding or formulating a research plan***

- To recognise the importance of preparation for a research proposal
- To discuss ten steps on the road to success
- To describe the structure of a research proposal
- To evaluate feedback from a submitted research proposal

#### ***Conducting a research investigation and analysing findings***

- To explain the importance of planning for research implementation
- To describe conducting and recording research investigations
- To discuss the analysis of results and the use of statistics

- To describe the drawing of conclusions from results

#### **Writing research papers to publish**

- To recognise the objectives to publish research results
- To recognise the initial preparation in writing research paper for publication
- To recognise the importance of all contents in a manuscript
- To recognise ethical considerations in medical research

#### **Delivering research findings as oral presentations**

- To recognise the importance of presenting research findings
- To provide guidance on preparing to present research findings
- To describe good practice in oral presentations
- To describe good practice in poster presentations

#### **Auditing Research and planning for the future**

- To describe audit
- To explain the process of auditing research
- To describe how audit findings should be recorded and analysed
- To discuss planning for the future

### **SECTION B: ANALYTICAL SECTION**

The Analytical section is sub-divided into 'Instrumentation and Methodology' and 'Analytes' represented as follows for Clinical Chemistry and Immunology. From this section you should aim to be able to discuss the method principle and potential advantages and limitations of instruments and analytical techniques commonly used in Core and

Specialist Clinical Laboratories. It is expected that practical experience and competence in the use of generic laboratory equipment, basic techniques and laboratory equipment will be acquired in the workplace as appropriate.

See Figure B1 for Hierarchical structure of Blood Sciences as related to Clinical Chemistry and Immunology section specifically related to the analytical component of the curriculum.

The clinical component is shown in yellow to demonstrate the relationship between the analytical and clinical sections; which is presented separately in section C.

#### **Section B1. Generic Laboratory Equipment: Learning Objectives**

**Be able to discuss the basic principle of use of generic laboratory equipment:**

- Balances
- Centrifuges
- Microscopes
- pH meters
- Quantities and Units
- Waterbaths

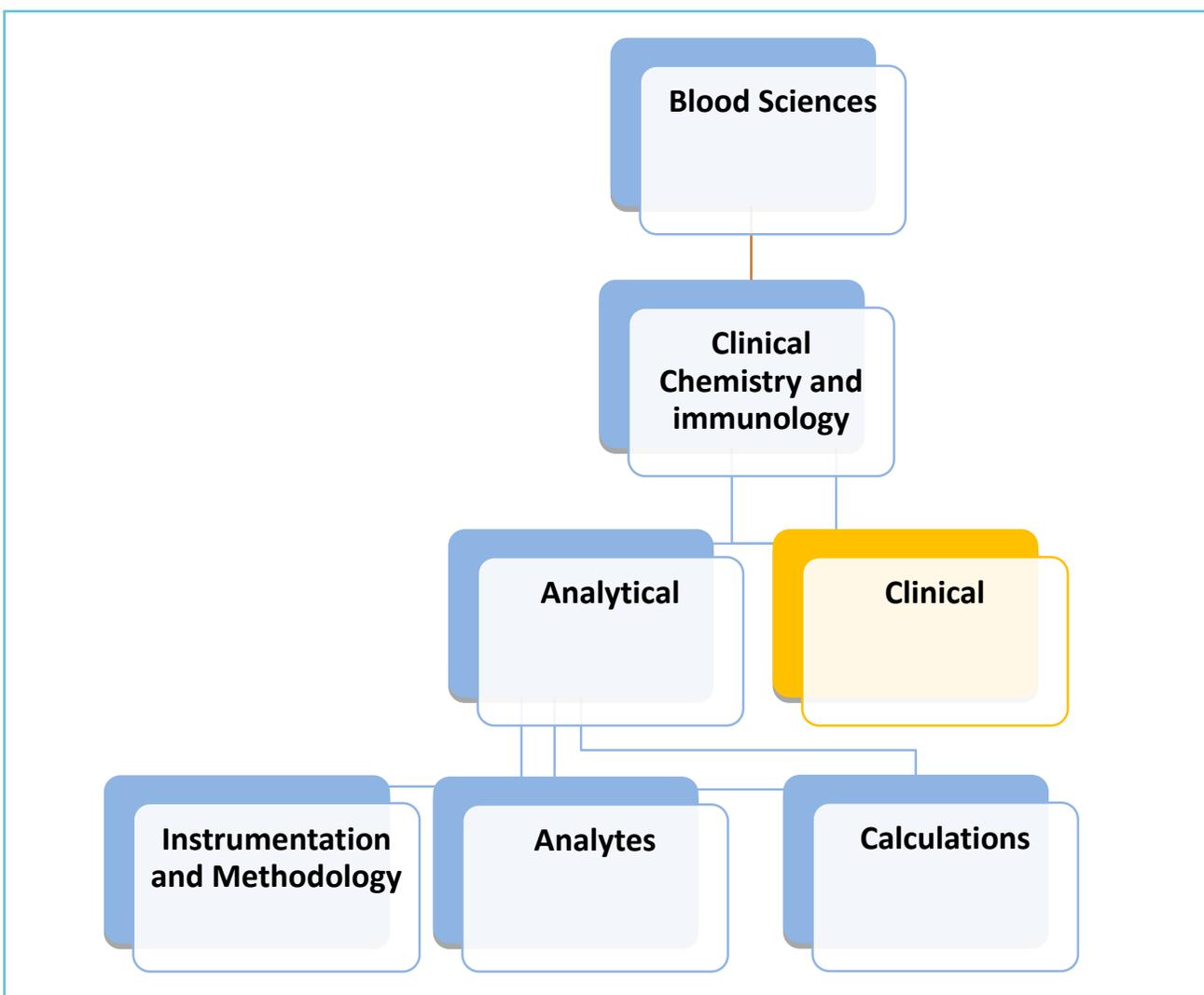
#### **Section B2. Basic Techniques: Learning Objectives**

**Be able to discuss the basic techniques as applied in laboratory medicine**

- Buffer preparation
- Calculations
  - ◇ Basic statistics of central tendency
  - ◇ Basic statistics of dispersion
  - ◇ Addition dilution
  - ◇ Serial dilution
- Centrifugation
- Dialysis

- Extraction techniques
  - ◊ Liquid-liquid
  - ◊ Solid Phase
  - ◊ Supported liquid
- Extractions
- Filtration
- Freeze drying
- Pipetting
- Ultrafiltration
- Volumetric measurement

**Figure B1** Hierarchical structure of Blood Sciences as related to Clinical Chemistry and Immunology (*related to the analytical component*)



**Figure B1:**

- Hierarchical structure of Blood Sciences as related to Clinical Chemistry and Immunology section specifically related to the analytical component of the curriculum.
- The clinical component is shown in yellow to demonstrate the relationship between the analytical and clinical sections; which is presented separately in section C.

- Weighing

### **Section B3. Laboratory Instruments – Routine: Learning Objectives**

**Be able to discuss the method principle and potential advantages and limitations of instruments and analytical techniques commonly used in a Core Laboratory**

- Absorption, nephelometry and turbidimetry
- Acid-base measurement
- Immunoassay and detection systems
- Ion selective electrodes
- Main analyser platforms and automation.
- Osmometry

### **Section B4. Laboratory Instruments – Spectroscopy: Learning Objectives**

**Be able to discuss the method principle and potential advantages and limitations of instruments and analytical techniques commonly used in Specialist Clinical Laboratories**

- Luminescence and fluorescence
- Spectrophotometry
- Spectrophotometry and ICP-MS
  - ◇ Atomic absorption
  - ◇ Flame emission photometry

### **Section B5. Laboratory Instruments – Electrophoresis: Learning Objectives**

**Be able to discuss the method principle and potential advantages and limitations of instruments and analytical techniques commonly used in Specialist Clinical Laboratories**

- Electrophoresis
  - ◇ 2-dimensional
  - ◇ Agarose
  - ◇ Capillary zone

- ◇ Cellulose acetate
- ◇ Isoelectric focusing (IEF)
- ◇ Immunofixation
- ◇ Isotachopheresis
- ◇ Polyacrylamide

### **Section B6. Laboratory Instruments – Chromatography: Learning Objectives**

**Be able to discuss the method principle and potential advantages and limitations of instruments and analytical techniques commonly used in Specialist Clinical Laboratories**

- Chromatography
  - ◇ Affinity
  - ◇ Column
  - ◇ Direct and reverse phase liquid chromatography
  - ◇ Gas chromatography
  - ◇ Gas vs liquid chromatography
  - ◇ High-performance liquid chromatography
  - ◇ Ion-exchange
  - ◇ High pressure liquid chromatography (HPLC)
  - ◇ Partition techniques
  - ◇ Planar
  - ◇ Principles of chromatography
  - ◇ Size exclusion techniques

### **Section B7. Laboratory Instruments – X-Mass Spectrometry: Learning Objectives**

#### **MS - Basic Concepts**

**Describe the basic principles of mass spectrometry (MS)**

**Explain the mass to charge ratio and mass spectra**

**Outline the components of a mass spectrometer, including ionisation sources (electron impact, chemical ionisation, electrospray ionisation), mass filters (quadrupole, magnetic), detectors**

- Mass spectrometry
  - ◊ Chromatographic separation (see above)
  - ◊ Gas Chromatography-MS (GC-MS)
  - ◊ Inductively Coupled Plasma MS (ICP-MS)
  - ◊ Liquid Chromatography MS (LC-MS)
  - ◊ LC-MS-MS
  - ◊ Matrix Assisted Laser Desorption/Ionization – Time of Flight (MALDI-TOF)

**Discuss the past, current and potential future clinical applications of mass spectrometers, including full scan, selective ion monitoring, multiple reaction monitoring, TOF**

### *Instrumentation*

**Critically discuss and compare mass spectrometry instruments in terms of their place in clinical testing along with advantage and limitations**

- GC- with single or tandem quadrupoles
- High- resolution MS
- ICP-MS
- LC-MS/MS with single or tandem quadrupoles
- MALDI-TOF
- Orbitrap
- Quadrupole – TOF (Q-TOF)

### *Principles of Analysis X-MS*

#### *Sample Preparation*

**Critically discuss the approaches to sample preparation in clinical testing along with advantage and limitations of each**

- Derivatisation

- Dilute and shoot
- Liquid-liquid extraction (LLE)
- Protein precipitation
- Supported liquid extraction (SLE)
- Solid phase extraction (SPE)

#### *Analytical – chromatography*

**Discuss the processes of chromatographic separation including the selection of columns and mobile phases**

**Define the terms isomer and epimer and explain the importance of chromatographic separation**

#### *Analytical - quality*

**Discuss the important considerations to support analytical quality**

- Calibrators including traceability and commutability
- External Quality Assurance (EQA)
- Interferences
- Internal quality control (IQC)
- Internal standard selection, including non-isotopic, deuterated and carbon 13
- Post implementation quality assessment
- Qualitative scans
- Quantifiers and qualifier selection
- Quantitation – calibration curves

#### *Post analytical*

**Discuss the implementation of mass spectrometry reference intervals**

**Outline the criteria for accepting an analytical run**

**Outline the requirements of reporting a result**

#### *Setting up a LC-MS/MS assay*

**Critically discuss the pre implementation quality assessment i.e. method validation required.**

**Critically discuss the role and selection of mass spectrometry instruments in terms of automation and processes.**

- Fully automated solutions
- Kit-user setting
- Lab developed tests
- Near patient testing
- Identification, optimisation, qualitative assessment, sample preparation to full quantitation

### *Applications*

**Discuss the clinical applications of mass spectrometry**

- Creatinine
- Drug of abuse testing
- Genomics
- Glycated haemoglobin
- Inborn errors of metabolism
- Metabolomics - Translation from discovery phase to targeted assays and clinical practice
- Microbiology
- Non-peptide hormones
- Peptide hormones
- Proteomics
- Therapeutic drug monitoring
- Toxicology including General unknowns screen – targeted MS/MS or high-resolutions MS
- Vitamins

**Discuss the application of mass spectrometry in a variety of clinical matrices**

- Blood including serum and plasma
- Dried blood spots
- Misc e.g. dried urine, dried saliva spots, hair, vitreous humour

- Saliva
- Urine

### *Section B8. Laboratory Instruments – Not otherwise classified: Learning Objectives*

**Be able to discuss the method principle and potential advantages and limitations of instruments and analytical techniques commonly used in Specialist Clinical Laboratories**

- Cell counters
- Emerging technologies,
  - ◊ Multiplex analysis
  - ◊ Nuclear magnetic resonance (NMR) spectroscopy
  - ◊ Sensors
- Enzymology
- Flow cytometry
- Isotopic techniques

### *Section B9. Analytes: Learning Objectives*

**Be able to identify the clinical relevance of each of these analytes (as applied in Section C)**

**Be able to discuss the basic methods, including their advantages and limitations, that could be used for the analysis of common analytes measured in laboratory medicine**

**Be able to discuss the matrix or matrices (including their advantages and limitations) used for measuring a particular analyte**

### *Lung*

- Base Excess
- Bicarbonate
- pCO<sub>2</sub>
- pH
- pO<sub>2</sub>

### **Renal**

- Aluminium
- Cystatin C
- Creatinine
- Inulin
- Potassium
- Sodium
- Urea
- Uric acid
- Urine albumin
- Urine creatinine
- Urine protein

### **Liver**

- Albumin
- Alkaline phosphatase (ALP)
- Alanine Aminotransferase (ALT)
- Aspartate Aminotransferase (AST)
- Bile acids
- Bilirubin
  - ◇ Total
  - ◇ Conjugated or Direct
  - ◇ Unconjugated or Indirect
  - ◇ Fractions
- Gamma-Glutamyl Transferase (GGT)
- Insulin like growth factor (IGF)-1
- Lactate dehydrogenase (LDH)
- Total protein

### **Metabolism**

- Ammonia
- Glucose
- Lactate
- HbA1c

### **Heart - muscle**

- B-type natriuretic peptide (BNP) and Pro-BNP
- Cholesterol
- Creatine kinase (CK)
- CK-MB
- High density lipoprotein (HDL)
- Low density lipoprotein (LDL)
- pCO<sub>2</sub>
- Triglycerides
- Troponin I
- Troponin T

### **Bone**

- 1,25 di hydroxy vitamin D
- Calcium
- Magnesium
- Phosphate
- Parathyroid hormone (PTH)
- Vitamin D (25 hydroxy vitamin D)

### **Endocrinology - Pituitary**

- Adrenocorticotrophic hormone (ACTH)
- Growth hormone (GH)
- Follicle stimulating hormone (FSH)
- Luteinizing hormone (LH)
- Thyroid stimulating hormone (TSH)

### **Endocrinology - Peripheral**

- 17 hydroxyprogesterone
- Aldosterone
- Anti-mullerian hormone (AMH)
- Cortisol
- Dehydroepiandrosterone (DHEA)
- DHEA sulfate (DHEA-S)
- Estradiol

- free triiodothyronine (fT3)
- free thyroxine (fT4)
- Insulin like growth factor I (IGF-I)
- IGF binding protein 3 (BP3)
- Inhibin
- Progesterone
- Steroid hormone profiles
- Sex hormone binding globulin (SHBG)
- Testosterone

#### ***Dynamic Function Tests***

- Dexamethasone suppression
- Glucagon stimulation Test
- Growth hormone releasing hormone (GHRH)-Arginine Test
- Insulin Tolerance Test
- Metyrapone Suppression Test
- Oral Glucose Tolerance Test (OGTT)
- OGTT for growth hormone (GH) suppression
- Synacthen stimulation
- Water deprivation

#### ***Gastrointestinal - nutrition***

- Amylase
- Ceruloplasmin
- Copper
- Faecal calprotectin
- Faecal elastase
- Ferritin
- Insulin
- Intestinal permeability
- Iodine
- Iron
- Lead
- Lipase

- Phorphyrin screen
- Selenium
- Vasoactive intestinal peptide (VIP)
- Vitamin A - retinol
- Vitamin B1
- Vitamin B2
- Vitamin B3
- Vitamin B6
- Vitamin B9 – folate
- Vitamin B12
- Vitamin C
- Vitamin D
- Vitamin E
- Vitamin K
- Transferrin
- Zinc

#### ***Biomarkers of Cancer***

- Alpha foeto protein
- 5-hydroxyindoleacetic acid (5HIAA)
- Carbohydrate antigen (CA) 19-9
- CA125
- Calcitonin
- Catecholamines
- Carcinoembryonic antigen (CEA)
- Chromogranin A
- Homovanillic acid (HVA)
- Prostate specific antigen (PSA)
- Thyroglobulin

#### ***Therapeutic Drug Monitoring and Toxicology***

- Acetaminophen (paracetamol)
- Carbamazepine
- Carbon monoxide

- Cyclosporine
- Digoxin
- Ethanol
- Ethylene glycol
- Lithium
- Mycophenolic acid
- Methanol
- Methotrexate
- Phenytoin
- Salicylate
- Saliva drug screen
- Sirolimus
- Tacrolimus
- Theophylline
- Urine drugs of abuse screening

#### **Immunology**

- Albumin
- Alpha-1-antitrypsin quantification, phenotyping and genotyping
- Beta -2 microglobulin
- C1 esterase inhibitor
- Total complement activity (CH50)
- Complement C3 and C4
- C-reactive protein (CRP)
- Cryoglobulins
- Full blood count
- Haptoglobin
- Hepatitis A, B and C serology
- HIV serology
- IgE and specific IgE
- Immunofixation electrophoresis (IFE)
- Immunoglobulins (IgA, IgG, IgM)
- IgD
- IgG subclasses
- Immunosubtraction/immunotyping
- Lymphocyte subsets
- Monoclonal protein quantification
- Oligoclonal banding (isoelectric focusing)
- Prealbumin (transthyretin)
- Rheumatoid factor
- Serum and urine protein electrophoresis
- Serum free light chains
- Total complement activity (CH50)
- Transthyretin (prealbumin)
- Tryptase

#### **Autoantibodies**

- Acetyl choline receptor
- Adrenal
- Antibodies associated with neurological diseases (paraneoplastic antibodies)
- Centromere
- Cyclic citrullinated peptide
- Double stranded DNA
- Endomysium
- Extractable nuclear antigens
  - ◊ SSA (Ro)
  - ◊ SSB (La)
  - ◊ Ribo nuclear protein (RNP)
  - ◊ Sm
  - ◊ Jo1
  - ◊ SCL70
  - ◊ Scl Sm
- Gliadin
- Glomerular basement membrane
- Intrinsic factor
- Liver

- ◇ Liver kidney microsomal
- ◇ Mitochondrial
- ◇ Smooth muscle
- Neutrophil cytoplasm (ANCA)
  - ◇ Myeloperoxidase
  - ◇ Proteinase 3
- Nuclear components (ANA)
- Ovary
- Pancreas
  - ◇ Glutamic acid decarboxylase
  - ◇ Insulin
  - ◇ Insulinoma antigen 2 (IA-2)
  - ◇ Zinc Transporter 8 (ZnT8)
- Skin
  - ◇ Basement membrane
  - ◇ Intercellular cement
- Thyroid
  - ◇ Microsomal
  - ◇ Peroxidase/microsomal
  - ◇ Thyroglobulin
  - ◇ TSH receptor
- Tissue transglutaminase

### **Section B10. Laboratory Calculations: Learning Objectives**

**Be able to discuss the process for calculating common equations relevant to laboratory medicine**

- Addition dilution
- Anion Gap
- Bicarbonate
- Converting between mass and molar units
- Corrected calcium
- Corrected sodium

- Estimated glomerular filtration rate (eGFR)
- Globulins
- INR
- LDL
- Osmol Gap (including calculated osmolarity)

**Be able to perform basic statical calculations used in the laboratory.**

**Be able to distinguish the appropriate statistical tests to employ based on the distribution of the data.**

- Bias
- Biological variation
- Evaluation of differences between populations
- Measures of central tendency
- Measures of dispersion
- Multiple of Median (MOM)
- Positive and negative predictive value
- Reference interval
- Recovery
- Sigma
- Uncertainty of measurement

### **Section B11. Standardization, Traceability and Harmonization Learning Objectives**

#### **Core topics**

**Understand why different methods for the same analyte give different results**

**Explain why reducing between-method variability is important**

**Describe traceability in laboratory medicine**

**List the stakeholders involved in achieving traceability in laboratory medicine together with their respective roles**

### *Advanced*

**Standardization in general vs standardization in the metrology of chemistry**

**Understanding the concept of “amount of substance” and its unit the mole**

**Understand the concept “measurand”**

**The meaning of comparisons in measurement**

**Traceability as a property of the measurement result**

**Standardisation in the analytical phase and in the pre-and post-analytical phases of the total testing chain**

**Harmonisation and the importance of commutability**

**Standardisation as a top-down regulatory process which is stable in time and space**

**Harmonisation as a bottom up consensus process based on commutable patient samples and with less stability than standardisation in time and space**

**Examples of harmonisation projects**

## **SECTION C: CLINICAL SECTION**

In laboratory medicine it is essential for professionals to have a sound understanding of both analytical tools to achieve the best clinical outcomes. It is therefore essential that laboratory professionals have a sound working knowledge of physiology and pathophysiology related to their testing area. This section of the curriculum details the clinical areas related to clinical chemistry and immunology as detailed in Figure C1.

### ***Section C1. Fluid and Electrolyte Disorders: Learning Objectives***

#### ***Basic Concepts***

**To understand the principles and control of fluid and electrolyte balance:**

- Clinical assessment of ECF volume
- Extracellular and intracellular fluid volumes
- Hormonal control of fluid and electrolyte balance (renin, angiotensin, aldosterone, ADH)
- Principles of correcting fluid and electrolyte losses

#### ***Disorders and disease states***

**To understand the causes, clinical signs and symptoms of the following features of disorders relating to fluid and electrolyte metabolism.**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Dehydration
- Diabetes insipidus
- Extracellular fluid (ECF) volume loss
- Hypernatremia
- Hyperkalemia and pseudohyperkalemia
- Hypokalemia
- Hyponatremia and pseudo hyponatraemia
- Shock
- Syndrome of inappropriate antidiuretic hormone (SIADH)

#### ***Specific Laboratory Investigations***

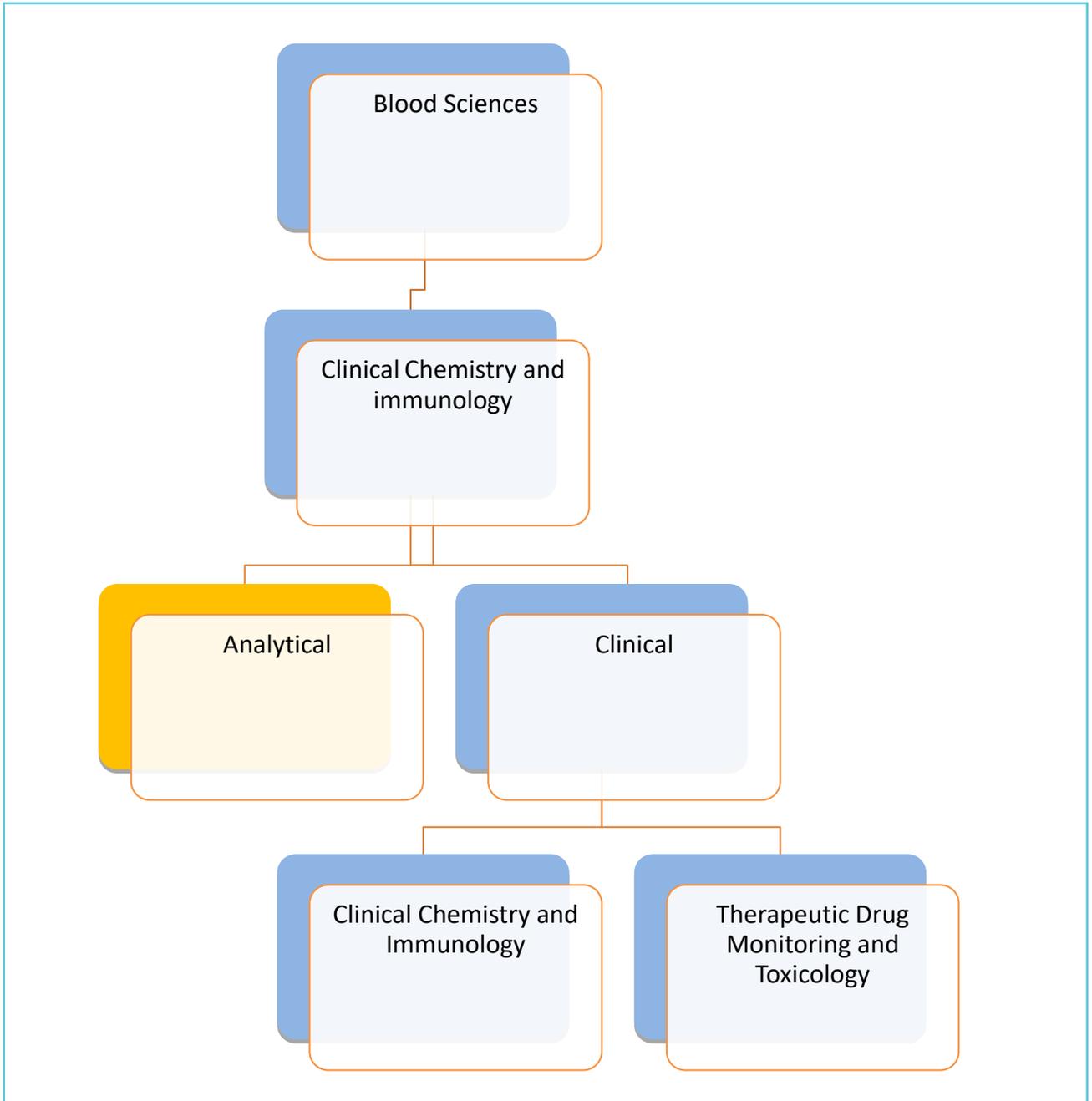
**To gain an in depth knowledge of the following specific laboratory investigations important to the study of fluid and electrolyte disorders.**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Aldosterone
- Electrolytes (sodium, potassium, chloride)

**Figure C1** Hierarchical structure of Blood Sciences as related to Clinical Chemistry and Immunology (*Clinical component*)



**Figure C1:**

- Hierarchical structure of Blood Sciences as related to Clinical Chemistry and Immunology section specifically related to the clinical component of the curriculum.
- The analytical component is shown in yellow to demonstrate the relationship between the analytical and clinical sections; which was presented separately in section B.

- Serum and urine osmolality
- Renin-angiotensin axis (RTA) assessment
- Urine and faecal electrolytes

### **Section C2. Acid-Base Regulation and Pulmonary Function: Learning Objectives**

#### **Basic Concepts**

**To understand the principles and control of acid – base balance and pulmonary function**

- Anion gap
- Compensation for acidosis and alkalosis
- Control of respiration
- Henderson-Hasselbach equation
- Haemoglobin dissociation curves and limitations of calculated oxygen saturation
- Osmol gap
- Systematic approach to investigating acid-base disturbances

#### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following features of disorders relating to acid-base balance and pulmonary function.**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Alpha 1 antitrypsin (A1AT) deficiency (*see also Section C7, Hepatobiliary disease*)
- Carbon monoxide poisoning
- Metabolic acidosis
- Metabolic alkalosis
- Pyloric stenosis
- Renal tubular acidosis (*see also Section 3, Disorders of kidney and urinary tract*)
- Respiratory acidosis

- Respiratory alkalosis

#### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of acid-base balance and pulmonary function.**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Alcohols (ethanol, methanol, ethylene glycol, isopropanol)
- Anion gap
- Blood gas and hydrogen ion measurements
- Co-oximetry (carboxyhaemoglobin and methaemoglobin)
- Calculated blood gas parameters and their limitations
- Ketones (urine and serum)
- Lactate
- Osmolality
- Osmol gap
- Salicylate

### **Section C3. Disorders of Kidney and Urinary Tract: Learning Objectives**

#### **Basic concepts**

**To understand the principles and control of renal function and the urinary tract, including renal stones and purine and pyrimidine metabolism**

- Clearance (creatinine, cystatin C, inulin)
- Creatinine standardisation
- Disorders and disease states

- Estimated glomerular filtration rate (eGFR) calculations
- Endocrine functions of the kidney
- Formation of renal calculi
- Haemodialysis
- Peritoneal dialysis
- Proteinuria; glomerular permeability, tubular proteinuria
- Renal stone formation
- Steady state renal function
- Transplant biochemistry

**To understand the causes, clinical signs and symptoms of the following features of disorders relating to renal function, the urinary tract and uric acid metabolism**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Acute kidney injury
- Amyloid
- Antineutrophil cytoplasmic antibodies (ANCA) associated vasculitis
- Chronic kidney disease
- Cryoglobulin associated renal damage
- Drug-induced renal damage
- Glomerulonephritis
- Goodpasture's syndrome
- Gout
- Hyperuricaemia
- Myeloma associated renal damage
- Nephritic syndrome
- Nephrotic syndrome
- Renal tubular acidosis (*see also Section 2: Acid-base regulation and pulmonary function*)

- Systemic lupus erythematosus (SLE)
- Urinary tract infection (UTI)
- Types of renal stone
- Uraemia
- Vasculitis (ANCA associated)

### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of renal function, the urinary tract and uric acid metabolism**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Antinuclear antibodies (ANA)
- ANCA
- Beta 2 microglobulin
- Complement C3 and C4
- Creatinine (serum and urine)
- Cryoglobulins
- Cystatin C
- Erythropoietin
- Examination and identification of renal calculi
- Measurement of immunosuppressant drugs (cyclosporine, tacrolimus, sirolimus)
- Phosphate, calcium and magnesium
- Renal calculi analysis
- Serum and urine electrophoresis and immunoglobulins
- Urea and urea kinetics
- Uric acid
- Urine albumin

- Urine dip stick analysis
- Urine microscopic analysis
- Urine oxalate

#### **Section C4. Immunology: Learning Objectives**

##### **Basic concepts**

**To understand the principles, components and control of the immune system**

**Components of the immune system (Cells, Lymphoid tissue, Soluble components and mediators)**

- Acute phase response
- Adaptive Immune system
- Complement
  - ◇ Alternative pathway
  - ◇ Classical pathway
  - ◇ Mannose-binding lectin (MBL) pathway
- Cytokines
  - ◇ Colony stimulating factors and haematopoietic
  - ◇ Interferons
  - ◇ Interleukins
  - ◇ Tumour necrosis factors
- Hypersensitivity reactions
  - ◇ Types I – IV (or V)
- Immunoglobulins
  - ◇ Function
  - ◇ Gene rearrangement
  - ◇ Structure
- Innate Immune system
- Lymphocytes
  - ◇ B lymphocytes
  - ◇ T lymphocytes

##### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following features of disorders relating to the immune system**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Allergy and anaphylaxis
- Autoimmune diseases
  - ◇ Endocrine
  - ◇ Gastro intestinal (GI) tract
  - ◇ Liver
  - ◇ Renal
  - ◇ Rheumatic and articular
  - ◇ Skin
- Lymphoid malignancy
  - ◇ B cell
  - ◇ T cell
- Primary immune deficiency
- Secondary immune deficiency
- Transplantation

##### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of disorders of the immune system**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Autoantibodies to
  - ◇ Skin basement membrane, intercellular cement

- ◇ Nuclear (ANA), smooth muscle, mitochondrial
- ◇ Neutrophil cytoplasmic (ANCA), glomerular basement membrane, ANA
- ◇ Rheumatoid factor, cyclic citrullinated peptides, nuclear, double stranded DNA, extractable nuclear antigens
- ◇ Thyroid, pancreas, adrenal, ovary, (testis)
- ◇ Tissue transglutaminase, endomysial, intrinsic factor
- Full blood count
- HLA typing
- Immunoglobulin quantification and IgG subclasses
- Lymphocyte subsets (CD3, 4, 8, 16/56, 19)
- Monoclonal protein identification and quantification in serum and urine
- Total and specific IgE
- Tryptase

### **Section C5. Diabetes Mellitus:** **Learning Objectives**

#### **Basic concepts**

**To understand the pathogenesis of diabetic states and the following aspects of the study of diabetes mellitus**

- Aetiology of Type 1, Type 2 and gestational diabetes
- Complications of diabetes (microvascular, macrovascular)
- Diabetic ketoacidosis
- HbA1c standardisation
- Guidelines for the screening, diagnosis and monitoring of diabetes
- Non-ketotic hyperosmolar coma

- Self-monitoring of blood glucose

#### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following aspects of diabetes mellitus**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Diabetic ketoacidosis
- Gestational diabetes
- Hypoglycaemia
- Metabolic syndrome
- Non-ketotic hyperosmolar coma
- Type 1 diabetes
- Type 2 diabetes

#### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of diabetes mellitus**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Anti-glutamic acid decarboxylase (GAD) antibodies
- Anti insulin antibodies
- Blood gas and hydrogen ion measurements
- C-peptide
- Fructosamine and other glycosylated proteins
- Glucagon
- Glucose
- Glucose tolerance tests
- HbA1c

- Insulin
- Insulinoma antigen 2 (IA-2)
- Ketones, ( $\beta$ -hydroxy butyrate)
- Microalbumin
- Zinc Transporter 8 (ZnT8)

### **Section C6. Gastrointestinal and Pancreatic Disease: Learning Objectives**

#### **Basic concepts**

**To understand the principles and control of gastrointestinal and pancreatic function**

- Acute and chronic pancreatitis
- Autoimmune bowel disease
- Bowel cancer screening
- Causes of gastric ulceration
- Endocrine and exocrine functions of the pancreas
- Inflammatory bowel disease
- Intestinal absorption of proteins, fats and carbohydrates
- Neuroendocrine Tumours
- Vitamin B12 absorption

#### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following features of disorders relating to gastrointestinal and pancreatic function**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Acute and chronic pancreatitis
- Carcinoid syndrome
- Coeliac Disease
- Crohn's Disease
- Food allergy

- H. pylori infection
- Intestinal malabsorption, including vitamins, (*see also Section 5 : trace elements and vitamins*)
- Neuroendocrine tumours
- Pyloric stenosis (*see also Section 2, Acid base regulation and pulmonary function*)
- Pernicious anaemia
- Zollinger-Ellison syndrome

#### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of disorders of gastrointestinal and pancreatic function**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- $^{14}\text{CO}_2$  urea breath test for H. pylori
- Amylase and macroamylase
- CA 19-9
- Carcinoembryonic antigen (CEA)
- Chromogranin A
- Elastase
- Endomysial autoantibodies
- Faecal calprotectin
- Faecal occult blood
- Hydrogen breath test for lactose intolerance
- IgE and specific IgE
- Intrinsic factor antibodies
- Lipase
- Serotonin and 5 HIAA
- Transglutaminase autoantibodies

- Vitamin B12 and folate
- Xylose absorption test

### **Section C7. Hepatobiliary Disease: Learning Objectives**

#### **Basic concepts**

**To understand the metabolic functions of the liver and the following aspects of hepatobiliary disease**

- Autoimmune disease
- Cholestasis
- Drugs – acute and chronic
- Genetic – e.g. A1AT deficiency (*see also Section 2, Acid-base regulation and pulmonary function*)
- Inflammatory and infective liver disease (hepatitis)
- Liver autoantibodies
- Liver cirrhosis
- Liver function – synthesis, conjugation, detoxification
- Liver transplantation
- Liver tumours – primary or secondary
- Origin, metabolism and transport of bilirubin

#### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following features of disorders relating to hepatobiliary function**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Acute hepatitis
- Alcoholic liver disease
- Allograft rejection
- Biliary damage and dysfunction

- Chronic hepatitis
- Cirrhosis ( Including primary biliary cirrhosis)
- Elevated bilirubin levels: conjugated, unconjugated and total
- Elevated neonatal bilirubin levels
- Infectious hepatitis
- Paracetamol (Acetaminophen) overdose

#### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of disorders of hepatobiliary function**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Albumin (blood and ascites)
- Alpha-1 antitrypsin concentration and phenotype/genotype
- Alphafoetoprotein (AFP)
- Ammonia
- Bile acids
- Bilirubin – conjugated, unconjugated, total, transcutaneous
- Caeruloplasmin
- Ethanol
- Ferritin
- Hepatitis serology
- Iron
- Liver enzymes: ALT, AST, ALP, GGT
- Measurement of immunosuppressant drugs (cyclosporine, tacrolimus, sirolimus)
- Paracetamol (Acetaminophen)
- PT-INR

## **Section C8. Lipids and Disorders of Lipoprotein Metabolism: Learning Objectives**

### **Basic concepts**

**To understand the principles and control of lipid metabolism and the following aspects of the study of lipid and lipoprotein disorders**

- Apolipoproteins: functions, receptors (e.g. LDL-R)
- Cardiovascular disease risk calculation and evaluation, and cost-effectiveness of lipid screening strategies.
- Fatty acid transport and oxidation
- Lipid absorption, transport and metabolism
- Lipoprotein metabolism: endogenous and exogenous pathways

### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following features of disorders relating to lipid and lipoprotein disorders**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Atherosclerosis
- Hypercholesterolaemia
- Hyperlipidemia
  - ◊ Inherited disorders
  - ◊ Non-inherited disorders
- Hypolipidemia
- Metabolic syndrome

### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of disorders of lipid and lipoprotein metabolism**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Apolipoprotein A and B
- Genotyping of ApoE, LDL receptor and LPL
- HDL cholesterol
- High sensitive CRP
- LDL cholesterol – direct and calculated methods
- Lipoprotein electrophoresis
- Lipoprotein ultracentrifugation
- Lp(a)
- Non-HDL cholesterol (calculated)
- Total cholesterol
- Triglycerides

## **Section C9. Cardiovascular Disorders and Hypertension: Learning Objectives**

### **Basic concepts**

**To understand the causes and manifestations of the cardiovascular disease the assessment of individual risk**

- Acute coronary syndrome
- Cardiac risk assessment
- Myocardial infarction

### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following features of cardiovascular disorders**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Atherosclerosis
- Cardiac amyloid

- Congestive heart failure
- Hypertension
- Myocardial infarction
- Stable angina
- Unstable angina

### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of cardiovascular disease and hypertension**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Anti-heart muscle antibodies (Dresslers)
- High-sensitivity CRP
- Natriuretic peptides
- Serum and urine electrophoresis and immunoglobulins
- Troponin and high-sensitivity troponin

### **Section C10. Calcium, Magnesium, Parathyroid, Bone Disorders: Learning Objectives**

#### **Basic concepts**

**To understand the control of calcium and phosphate homeostasis including the following specific aspects of the process.**

- Circulating forms of calcium
- Metabolism of vitamin D
- Markers of bone resorption and bone formation
- Primary versus secondary hyper/hypocalcaemia

- Regulation of calcium and phosphate levels

### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following disorders and manifestations of calcium and phosphate metabolism and bone disease**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Hypercalcaemia
- Hypermagnesaemia
- Hyperparathyroidism
- Hyperphosphataemia
- Hypocalcaemia
- Hypomagnesaemia
- Hypoparathyroidism
- Hypophosphataemia
- Hypophosphatasia
- Pseudohypoparathyroidism
- Osteogenesis imperfecta
- Osteoporosis
- Paget's disease

### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of calcium and phosphate metabolism and bone disease**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- 1,25 di-hydroxy vitamin D
- 25 hydroxy vitamin D

- C- and N-telopeptides
- Calcium – total and ionized
- Magnesium
- Osteocalcin
- Phosphate
- PTH
- PTHrp
- Pyridinolines
- Total and bone-specific ALP

**Section C11. Iron and Haemoglobin Disorders, including the Porphyrin's:**  
**Learning Objectives**

**Basic Concepts**

**To understand the control and metabolism of iron and haem, the mechanisms which lead to iron overload and deficiency, and the implications of these states.**

**To understand the enzymatic defects of haem synthesis which lead to the porphyrias**

- Haem biosynthesis
- Haem metabolism
- Iron absorption, transport and storage
- Iron deficiency
- Iron overload

**Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following aspects and manifestations of disorders of iron and haem metabolism**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Acute and chronic porphyrias and their differential diagnosis
- Anaemia secondary to malignancy

- Glucose-6-phosphate dehydrogenase (G6PD) deficiency
- Haemochromatosis
- Haemoglobinopathies
- Intravascular haemolysis
- Iron deficient anaemia
- Thalassaemia

**Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of iron and haem metabolism and the porphyrias**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Delta-aminolaevulinic acid (ALA)
- Ferritin
- Full blood count
- G6PD
- Haptoglobin
- Haemoglobin and haemoglobin variants
- Haemopexin
- Iron
- Porphobilinogen (PBG)
- Porphyrins
- Soluble transferrin receptor
- Total iron binding capacity
- Transferrin
- Transferrin saturation

## **Section C12. Vitamins and Trace Elements: Learning Objectives**

### **Basic Concepts**

**To understand the importance of trace elements and vitamins to metabolic processes and wellbeing, the mechanisms of their actions and the consequences of deficiency and overload states.**

- Essential and non-essential metals
- Fat soluble vitamins; A and carotene, D, E and K
- Folate metabolism and function
- Genetic disorders of copper metabolism
- Genetic disorders of iron metabolism
- Potential vitamin toxicity
- Toxic and non-toxic metals
- Vitamin B12 absorption, metabolism and function
- Water soluble vitamins; B group vitamins and C

### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following aspects of disorders of trace element and vitamin metabolism**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Cadmium poisoning
- Copper deficiency/excess
- Folate deficiency
- Iron overload
- Lead poisoning
- Mercury poisoning
- Vitamin B12 deficiency

### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of trace elements and vitamins**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Cadmium in blood and urine
- Caeruloplasmin
- Delta amino laevulinic acid (ALA)
- Ferritin
- Folate
- Homocysteine
- Intrinsic factor antibody
- Laboratory assessment of specific B vitamin status
- Lead in blood and urine
- Mercury in blood and urine
- Methylmalonic Acid (MMA)
- Serum and urinary iron
- Serum and urinary copper
- Transferrin
- Vitamin B12
- Vitamin D

## **Section C13. Pregnancy and Prenatal Diagnosis: Learning Objectives**

### **Basic Concepts**

**To understand the following concepts in relation to the provision of a clinical laboratory service to support pregnancy and the health of the mother and foetus.**

- Biochemical, haematological and endocrine changes during pregnancy
- Changes in analyte levels throughout pregnancy
  - ◊ Multiples of the median
- Foetal lung maturity
- hCG doubling time
- hCG forms
- Maternal serum screening – purpose, limitations, screen vs. definitive testing
  - ◊ First trimester screening
  - ◊ Integrated screening
  - ◊ Second trimester screening
- Premature rupture of membranes and pre-term labour
- Rh isoimmunisation

#### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following, complications of pregnancy and foetal development.**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Choriocarcinoma
- Ectopic pregnancy
- Gestational diabetes
- Molar pregnancy
- Obstetric cholestasis
- Open neural tube defects
- Pre-eclampsia, HELLP syndrome
- Rh isoimmunisation
- Trisomy 21, 18 and 13
- Trophoblastic disease

#### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of pregnancy and foetal development**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- AFP
- hCG
- Inhibin A
- PAPP-A
- Plasmic nucleic acids
- Serum bile acids
- Unconjugated estriol

**To be able to discuss the clinical rationale for tests using amniotic fluid**

- Acetylcholinesterase
- AFP
- Bilirubin – absorbance at 450 nm
- Karyotype

#### **Section C14. General Paediatric Clinical Chemistry: Learning Objectives**

##### **Basic Concepts**

**To understand the following special considerations in relation to the provision of a general paediatric clinical laboratory service.**

- How to collect heel prick samples
- Issues with capillary specimens
- Paediatric reference intervals – dynamic changes with growth, development and puberty

- Sample volume and collection issues, including sweat collection

### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the conditions which may present to a general paediatric laboratory.**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Congenital thyroid disease
- Cystic fibrosis
- Delayed puberty
- Diabetes mellitus type 1
- Disorders of sex development, including congenital adrenal hyperplasia
- Growth retardation and growth hormone deficiency
- Hypocalcaemia
- Inborn errors of metabolism
- Neonatal hypoglycaemia
- Neonatal jaundice
- Neuroblastoma
- Precocious puberty
- Respiratory distress

### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of disorders presenting in the neonate and in childhood**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

**For all analyses, sample size is of key importance in method selection**

- Acid base / blood gases
- Calcium
- Glucose
- Hormone measurement (*see Section 16, Endocrinology*)
  - ◊ Anterior hypothalamic hormones
  - ◊ Cortisol
  - ◊ Neuropeptides
  - ◊ Ovarian hormones
  - ◊ Testicular Hormones
  - ◊ Thyroid function
  - ◊ Other adrenal hormones
- HVA, dopamine
- Performance of the sweat test
- Plasma catecholamines
- Total and differential bilirubin

### **Result interpretation**

**To recognise that the population-based reference intervals for many of children's chemistries change throughout childhood.**

**To recognise that these reference intervals change differently for different analytes.**

**To recognise some of the problems associated with reporting children's chemistries.**

**To be aware of some of the problems that arise from failing to report correct children's chemistry reference intervals**

### **Section C15. Inborn Errors of Metabolism: Learning Objectives**

#### **Basic Concepts**

**To understand all aspects of screening for disease including the rationale for screening and the process.**

- Challenges with newborn screening
- Diseases appropriate for newborn screening – characteristics
- Newborn screening process

#### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following inherited conditions**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Congenital hypothyroidism
- Cystic fibrosis
- Enzyme deficiencies: biotinidase, galactokinase
- Fatty acid oxidation disorders: short, medium, long and very long chain
- Haemoglobinopathies
- Homocystinuria
- Lysosomal disease, glycogen storage diseases: lipidoses, hexosaminidases, Fabry's disease
- Maple syrup urine disease
- Phenylketonuria
- Tyrosinaemia

#### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of inherited metabolic diseases**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Acylcarnitines
- Alpha-1-antitrypsin genotyping
- Amino acids
- Haemoglobin electrophoresis
- Immunoreactive trypsinogen
- Organic acids
- Specific enzyme testing (e.g., biotinidase, galactokinase)
- Sweat chloride and conductivity

### **Section C16. Endocrinology: Learning Objectives**

#### **Basic Concepts**

**To understand all aspects of hormone action, including feedback inhibition and other controlling mechanisms for hormone release and to acquire a detailed knowledge of the major endocrine organs and systems.**

#### **Hypothalamic-pituitary axis**

- Anterior pituitary hormones
- Communication between pituitary and hypothalamus – anterior vs. posterior
- Hirsutism and virilisation
- Hypothalamic hormones
- Inhibitory hormones
- Posterior pituitary hormones
- Primary vs. secondary causes
- Renin-angiotensinogen-aldosterone pathway
- Steroid biosynthesis pathway
- Stimulation tests

- Suppression tests

### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following endocrine disorders**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Acromegaly/gigantism
- Addison's syndrome
- Adrenal insufficiency
- Congenital adrenal hyperplasia
- Cushing's syndrome and Cushing's disease
- Female infertility
- Growth hormone deficiency
- Hyperaldosteronism
- Hyperprolactinemia
- Hyperthyroidism
- Hypothyroidism
- Male infertility
- Pheochromocytoma
- Polycystic ovarian syndrome
- Premature ovarian failure
- Sheehan's syndrome
- Thyroid cancer
- 17 hydroxyprogesterone
- ACTH
- ADH
- Aldosterone, renin and ratio
- Androstenedione
- Angiotensin converting enzyme (ACE)
- Autoantibodies to the relevant endocrine organ
- Catecholamines (plasma and urine)
- Cortisol – serum, urine, salivary
- Dexamethasone suppression test
- DHEAS
- Estradiol
- FSH
- Growth hormone
- Growth hormone suppression test (OGTT)
- Insulin-like growth factor 1 (IGF-1)
- LH
- Metanephrines (plasma and urine)
- Progesterone
- Prolactin and macroprolactin
- SHBG
- Testosterone – total, free, bioavailable
- Thyroglobulin, anti-thyroglobulin antibodies
- Thyroid function tests: TSH, Free T3, free T4  
Total T3, Total T4
- TSH receptor antibodies

### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of endocrine disorders**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

### **Section C17. Neurological and Psychiatric Disorders: Learning Objectives**

#### **Basic Concepts**

**To understand the following key concepts relating to neurological processes and disruption of these**

- Blood brain barrier
- Paraneoplastic syndromes

### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following disorders, some of which are primary neurological disorders and some of which have neurological manifestations**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Acute porphyria's
- Alzheimer's disease
- Meningitis
- Multiple sclerosis
- Myasthenia gravis
- Paraneoplastic syndrome

### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important to the study of neurological disorders**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Aminolaevulinic acid (ALA)
- Anti-acetylcholine receptor antibodies
- Anti-Hu, Anti-Yo antibodies
- CSF beta-2-transferrin in rhinorrhoea and otorrhoea (fistula)
- CSF glucose
- CSF protein
- Examination of synovial fluid

- Oligoclonal banding (isoelectric focusing)
- Paraneoplastic antibodies
- Porphobilinogen (PBG)
- Porphyrins (urine, feces, serum)

### **Section C18.**

### **Biochemical Aspects of Monitoring Malignant Disease: Learning Objectives**

#### **Basic Concepts**

**To understand the following key concepts relating to the choice, use and measurement of biomarkers of cancer**

- Characteristics of an ideal biomarkers of cancer
- Uses and limitations of current biomarkers of cancer
- Uses of biomarkers of cancer: prognosis, monitoring, recurrence

#### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important in the management of malignant diseases**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- AFP
- ALP isoenzymes
- CA 15-3
- CA 19-9
- CA 125
- Calcitonin
- CEA
- HE4

- hCG
- HER2/Neu
- LDH isoenzymes
- Mammary specific antigen
- PSA (total and free)
- PTHrp
- Protein electrophoresis
- Thyroglobulin, anti-thyroglobulin antibodies
- Other emerging biomarkers as deemed relevant

### **Section C19. Musculoskeletal Diseases: Learning Objectives**

#### **Basic concepts**

**To understand muscle function and the use and limitations of autoimmune testing in diagnosis**

- Autoimmune testing
- Muscle function

#### **Disorders and disease states**

**To understand the causes, clinical signs and symptoms of the following musculoskeletal disorders**

**To describe which laboratory investigations are important in their detection, diagnosis and management**

- Duchenne / Becker dystrophy
- Osteoarthritis
- Rhabdomyolysis
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Vasculitis

#### **Specific Laboratory Investigations**

**To gain an in depth knowledge of the following specific laboratory investigations important in the management of musculoskeletal diseases**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Anti-CCP antibodies
- Anti-ds DNA
- Anti-neutrophilic cytoplasmic antibodies (ANCA)
- Anti-nuclear antibodies (ANA and specific antibodies SSA, SSB, Sm, RNP)
- Rheumatoid factor
- Serum creatine kinase

### **Section C20. Therapeutic Drug Monitoring and Toxicology: Learning Objectives**

#### **Basic Concepts**

**To understand the following key concepts of pharmacology and the key factors relevant to drug action and measurement.**

**To understand the mode of action and clinical uses of drugs in the categories listed.**

#### **Pharmacokinetics (PK)**

- Absorption
- Bioavailability
- Compliance
- Distribution
- Excretion
- Metabolism
- Peak vs. trough drug levels
- Steady state

#### **Pharmacodynamics (PD) and Pharmacogenetics (PG)**

- Antibiotics
- Antidepressants

- Anti-epileptic drugs
- Anti-psychotic drugs
- Carbon monoxide poisoning
- Cardioactive drugs
- Common drugs of abuse
- Drugs appropriate for TDM
- Drug screens vs. confirmatory tests for drugs of abuse
- Free drugs
- Immunosuppressants
- Lithium
- Methotrexate and rescue
- Thiopurines
- Warfarin

#### *Disorders and disease states*

**To understand the causes, clinical signs and symptoms of the following toxic conditions and the treatment regimes which may be used,**

**To describe which laboratory investigations are important in their diagnosis and management**

- Acetaminophen toxicity
- Carbon monoxide poisoning
- Ethanol, alcohol toxicity
- Organophosphate poisoning
- Salicylate toxicity

#### *Specific Laboratory Investigations*

**To gain an in depth knowledge of the following specific laboratory investigations important in for drug monitoring and detection of toxic concentrations of drugs**

**To be familiar with analytical methods available for their measurement**

**To be able to select laboratory investigations and interpret the analytical results in the light of the clinical signs and symptoms in the individual patient**

- Acetaminophen
- Carbon monoxide – carboxyhaemoglobin
- Cholinesterase and pseudocholinesterase
- Cyclosporine
- Ethanol
- Ethylene glycol
- Isopropanol
- Methanol
- Mycophenolic acid (MPA)
- Osmolality
- Point-of-care drug screens
- Sirolimus
- Salicylates
- Tacrolimus



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