# Training Syllabus

## LABORATORY SYLLABUS


**Syllabus for Training in Inborn Errors of Metabolism for Scientists and Medically Qualified Laboratory Staff**

This syllabus is intended as a guide. Whilst the training should be comprehensive, it is recognised that not all subjects can be covered in the same detail. Changes may also be necessary to meet local needs.

| Knowledge | Skills | Attitude |
|---|---|---|
| Physiology and Biochemistry | Investigative skills | Professional |
| Knowledge of Laboratory Procedures | Technical Skills | Communication |
| Knowledge of Paediatric Metabolic Disease | Management skills | Education |
| Ethics | Academic skills | Support |
| | Teaching skills | Academic/Research |
| | Organisational skills | Managerial |
| | Research skills | |

APPENDIX: INBORN ERRORS OF METABOLISM

### L.1 KNOWLEDGE

#### *L.1.1 Physiology and Biochemistry*

**Basic biochemistry.**

Structure/function relationships of the cell

- membranes, nucleus, cytoplasm, Golgi apparatus, endoplasmic reticulum, mitochondria, lysosomes, peroxisomes.

Enzymes/proteins

- the nature of proteins and enzymes, structure/function relationships, cellular distribution, function, mechanisms of action, control of enzyme activity, synthesis, processing, targeting, turn-over, measurement principles.

Mechanisms of inheritance and an understanding of molecular genetics

- molecular basis of gene expression, gene to protein pathways, the genetic code, mutations in genes, transcription, translation, post transcriptional modification, post translational modifications, effects of mutations on proteins/enzymes, analysis of mutations, frequency of genetic diseases, heterozygote detection, principles of prenatal diagnosis, population genetics, inheritance patterns,basic linkage (RFLP) analysis, mitochondrial DNA.

**The normal physiology and biochemistry, including changes during childhood, of:**
**fluid and electrolyte balance.**

- acid - base regulation
- intermediary metabolism including blood glucose and metabolic response to fasting, lactate, ammonia, aminoacids, organic acids and fatty acids.
- oxidative phosphorylation and the respiratory chain
- lipids and lipoproteins
- cholesterol and other sterols
- lysosome and peroxisome metabolism
- purines and pyrimidines
- porphyrins
- calcium metabolism

- bilirubin
- trace metal metabolism
- relevant aspects of brain metabolism including neurotransmitters. The role of the blood brain barrier
- enzyme biochemistry and tissue expression

***L.1.2 Knowledge of Laboratory Procedures***

- reagent preparation, storage and handling
- sample preparation, isolation, concentration, purification
- stability/storage of patient tissues and other specimens
- cell/organelle isolation
- bioassays
- spectrophotometry
- fluorimetry
- luminescence
- immunoassay
- radionuclides (including safety)
- electrophoresis and related techniques (eg, isoelectric focussing)
- gas chromatography
- HPLC
- mass spectrometry
- cell culture
- protein chemistry
- DNA extraction and banking
- PCR, Southern, Northern, Western analysis
- ASO mutation detection (ARMS)
- mutation detection/screening

***L.1.3 Knowledge of Paediatric Metabolic Disease***

- The pathological and biochemical changes, clinical symptoms, investigations and management in metabolic disorders of these pathways and organelles, as listed in the appendix.
- Treatment measures. An understanding of the measures used for the treatment of metabolic disorders including:
    - dietary management, metabolic inhibitors, metabolic activators, plasma exchange/plasmapheresis, chelation, organ transplantation, enzyme replacement, gene therapy

***L.1.4 Ethics***

- Ethics of research in research
- Process of informed consent
- Issues governing the ethics and consent for trials

**L.2. SKILLS**

***L.2.1 Investigative skills***

Laboratory investigation of metabolic causes of :

- Acute encephalopathy
- Neurological disease to include retardation, regression, fits, movements disorder, myopathy, etc
- Liver disease including acute liver failure
- Hepatosplenomegaly
- Cardiomyopathy
- Eye disease
- Nutritional status and growth
- Dysmorphic patients
- Skeletal disorders
- Skin disorders
- Renal disorders including the Fanconi syndrome
- Muscle disease

***L2.2 Technical Skills***

**Investigations of inborn errors of metabolism. Experience and understanding of the principles and performance of methods and interpretation of results with emphasis on defects of:**

- amino acid metabolism, (incl. ammonia)

- organic acid metabolism
- carbohydrate metabolism and glucose homeostasis (glucose,FFA,lactate,ketones)
- fatty acid oxidation (carnitines)
- fat metabolism
- purines and pyrimidine metabolism
- neurotransmitter and biogenic amine metabolism (CSF and other fluids)
- vitamin and coenzyme metabolism
- peroxisomal disorders (VLCFA,pristanoate, phytanate,etc)
- mitochondrial disorders
- lysosomal disorders
- glycosylation disorders:
  hereditary disorders of electrolyte and trace element metabolism including calcium, phosphate and magnesium , forms of rickets and osteopenias.

**Laboratory diagnostic experience. Interpretation of obtained data is an essential part of the diagnostic task.**

- Diagnosis at the metabolite level
  - Chemical diagnosis of defects of intermediary metabolism, storage diseases and monitoring of treatment
  - simple screening tests and TLC
  - gas chromatography/mass spectrometry for organic acid analysis
  - automated amino acid analysis
  - specialist assays of intermediary metabolites and carnitine
  - loading and function tests
    - fasting test for disorders of intermediary metabolism
    - allopurinol test
    - glucagon test
    - tests for co-factor responsive disorders (such as B12 test for MMA)
    - protein, amino acid, MCT,LCT, glucose loading
- Diagnosis at the enzyme level
  - Determination of enzyme activities
  - tissue culture and enzyme assay for selected disorders
  - white cell enzyme assays
- Diagnosis at the DNA level
  - protein and DNA analysis byblotting techniques, PCR and related methods.
- Techniques of whole population neonatal screening for phenylketonuria, neonatal hypothyroidism and other disorders including interpretation of test results and involvement in follow-up testing.

**Quality assurance:**

- Quality assessment and accreditation according to accepted norms such as ISO 9000, CCKL guidelines and good laboratory practice.
- Standardisation, calibration and evaluation of analytical techniques.
- Technical performance schemes and proficiency testing.

**Experience of patient care including:**

- attendance at ward rounds in General Paediatrics and Neonatal Special Care
- attendance at relevant specialist clinics
- participation in clinical care of patients with inborn errors of metabolism as a consultant to clinical colleagues.

***L.2.3 Management skills***

- Understanding of management skills required for development and use of resources in the metabolic laboratory, including budget control, contracting, strategic planning and writing a business plan.
- Experience of day to day running of a paediatric metabolic laboratory service, occupational health and safety matters, chemical safety, radiation safety, physical safety, biohazards and related legislation
- Human resources management including staff selection, training and conflict resolution
  Structure and function of local, regional and national health provision organisation

***L.2.4 Academic skills***

- Critical evaluation of scientific and laboratory results from literature review and audit
  An understanding of the methods used to establish evidence based practice
- Manuscript preparation
- Oral presentation skills

### *L.2.5 Teaching skills*

- Formal and informal teaching skills at undergraduate and postgraduate level
- Development of core teaching material to enable participation in teaching programmes on a regular basis
- Organisation of scientific teaching programmes

### *L.2.6 Organisational skills*

- Routine departmental tasks including duty rotas, teaching programmes and postgraduate meetings

### *L.2.7 Research skills*

- Design of scientific studies including medical statistics and grant application preparation
- Data organisation and presentation
- Computer literacy

## L.3. ATTITUDES

### *L.3.1 Professional*

- Appreciate the patient and families and non-specialist colleagues understanding of metabolic disease
- Working in partnership with others who care for the children such as multi disciplinarianteams and parent groups

### *L.3.2 Communication*

- Effective communication and appropriate approach to clinical, nursing and supplementary health professionals, general medical and university colleagues, pathology staff and hospital managers.

### *L.3.3 Education*

- Commitment to continuing self-education and to teaching others

### *L.3.4 Support*

- Understanding and positive approach to the supervision of junior laboratory staff
- Recognition of and coping with stress in self and others

### *L.3.5 Academic/Research*

- Innovative attitude to scientific problems
- supportive to / active in research
- Collaborative attitude to local, national and international colleagues

### *L3.6 Managerial*

- Interest in the overall organisation of departmental activities
- Understanding approach to local management structure
- Constructive attitude to the process of decision making
- Acceptance of shared responsibility for the use of resources
- Ability to respond effectively to laboratory related complaints

## APPENDIX
## INBORN ERRORS OF METABOLISM

- Disorders of aminoacid and peptide metabolism
- (Phenylketonuria including the management in pregnancy, homocystinuria, MSUD, etc)
- Disorders of organic acid metabolism (propionic acidaemia,methylmalonic acidaemia,etc)
- Hyperammonaemia and urea cycle disorders
- Disorders of carbohydrate metabolism (Glycogen storage disease, galactosaemia, fructosaemia,etc)
  Disorders of fatty acid oxidation (MCAD,LCHAD, etc)
- Disorders of ketone body metabolism
- Lysosomal storage disorders (MPS, etc)
- Disorders of lipoproteins and lipid metabolism

- Peroxisomal disorders (Adrenoleucodystrophy,Zellweger’s syndrome,etc) Disorders of purine and pyrimidine metabolism
- Disorders of calcium metabolism
- Disorders of metal metabolism (Wilson’s disease, Menkes syndrome,etc)
  Congenital lactic acidoses and metabolic myopathies
- Porphyrias
- Disorders of cholesterol,sterol and bile acid metabolism
- Disorders of vitamin metabolism (biotin,cobalamin,etc)
- Defects of membrane transport (lysinuric protein intolerance,etc)
- Defects of glycosylation
- Defects of connective tissue