

SYLLABUS FOR TRAINING IN CLINICAL PAEDIATRIC METABOLIC MEDICINE

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. Non-core subjects are indicated by an asterisk * but trainees may still wish include these. Changes may also be necessary to meet local needs.

Prerequisite: It is essential that those wishing to train in paediatric metabolic medicine should have sound basic training in paediatrics to include normal growth and development as well as the diagnosis and management of common disorders at all ages.

A. BASIC KNOWLEDGE

i). 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

The pathological and biochemical changes, clinical symptoms, investigations and management in metabolic disorders of these pathways and organelles.

ii). The normal nutritional requirements of protein, energy, vitamins and minerals for normal growth and development.

The principles of dietary therapy including the consequences of changes in the intakes of nutrients. Consequences of under-nutrition and specific nutritional deficiencies.

iii). Mechanisms of inheritance and an understanding of molecular genetics including mitochondrial DNA

Understanding of principles of prenatal diagnosis

Understanding the principles of gene therapy

iv) Normal intellectual and psychological development

An understanding of the methods used to assess DQ, IQ, behaviour and neuropsychological function

B. CLINICAL SKILLS

i). Assessment and investigation of metabolic causes of :

1. Acute encephalopathy
2. Neurological disease to include retardation, regression, fits, movements disorder, myopathy, etc
3. Liver disease including acute liver failure
4. Hepatosplenomegaly
5. Cardiomyopathy
6. Eye disease
7. Abnormal nutritional status and growth
8. Dysmorphic patients
9. Skeletal disorders
10. Skin disorders
11. Renal disorders including the Fanconi syndrome

ii). Emergency management and indications for and *the use of:

assisted ventilation
peritoneal dialysis
haemodialysis, haemofiltration and related techniques
intracranial pressure monitoring

iii). Genetic counselling and *counselling prior to prenatal diagnosis

C. TECHNICAL SKILLS

1. Interpretation of the investigations including understanding analytical, physiological and nutritional factors that influence the results. The use of investigations for long term monitoring of metabolic disorders.

Aminoacids

*Neurotransmitter and biogenic amine metabolites in CSF and other fluids

Organic acids (including interpretation of GC/MS data)

Ammonia

Intermediary metabolites: glucose, FFA, lactate, ketones, counter-regulatory hormones

Carnitines

*Enzymes studies: specific and non specific assays

Glycosaminoglycans

*Lipids and lipoproteins

Peroxisomal enzymes and metabolites (VLCFA, pristanate. Phytanate ,etc)

*Purines and pyrimidines

*Vitamin, mineral and other nutrient analyses including copper and caeruloplasmin

2. Indications and interpretation of:

fasting test for disorders of intermediary metabolism
allopurinol test
glucagon test
tests for co-factor responsive disorders (such as B₁₂ test for MMA)
*loading tests, protein, aminoacid, MCT,LCT, glucose
screening tests

3 Biopsies

a). indications for, planning and interpretation of assays arising from:

skin biopsy (for fibroblast culture)
liver biopsy
muscle biopsy
*and other biopsies

4. Experience of the use and interpretation of molecular genetic techniques

5. Practical aspects of dietary management:

evaluation of nutritional intake and requirements
low protein diets and those with controlled aminoacid intake (MSUD,PKU)
low and very low fat diets
diets for peroxisomal disorders including adrenoleucodystrophy
galactose and fructose free diets
dietary management of glycogen storage disease
emergency /crisis regimens
electrolyte replacement regimens (for treatment of Fanconi syndrome)

6. Interpretation of psychological and neuropsychometric testing

D. ATTITUDES

- i). Appreciate the patient and families understanding of metabolic disease
- ii). Understanding of psychological stress of diagnosis of metabolic disorders
- iii). Understanding of ethnic and cultural differences in attitudes to metabolic disorders.
- iv). Understanding of the problems for the patient and family of progressive disorders and disorders in which the natural history is very difficult to predict (for example Leighs disease).
- v). Working in partnership with others who care for the children to include multidisciplinary teams, education authorities, etc.

E. PARTICULAR PROBLEMS

1.Understanding of all aspects of the diagnosis and management of:

Disorders of aminoacid and *peptide metabolism

(Phenylketonuria, 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 (lysine protein intolerance, etc)
 Defects of glycosylation
 *Defects of connective tissue

2. Drug management.

An understanding and experience of the drugs used for the treatment of metabolic disorders.

*3. Transplantation, enzyme replacement and gene therapy

The metabolic indications for and long term follow up of

liver transplantation
 bone marrow transplantation
 renal transplantation

The use and indications of enzyme replacement therapy

The current status of gene therapy