Curriculum for Pediatric Chemical Pathology (Red Cross Children's Hospital Rotation)

Core knowledge:

Physiology and Biochemistry

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

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.

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

· Transplantation. The metabolic indications for and long term follow up of

1. liver transplantation

2. haematopoietic stem cell transplantation

3. renal transplantation

· Principles of *ex vivo* and *in vivo* gene transfer and its relevance to IEM

Diagnostic procedures in Paediatric Metabolic Disease

Newborn screening protocols – single disease screening on cord blood or dried blood spots (thyroid, PKU, Galactosaemia), Tandem MS screening for multiple disorders

Amino Acid Analysis by HPLC

Organic Acid Analysis by Gas Chromatography

Selected serum, red cell, leukocyte and fibroblast
manual enzyme assays using colorimetric, fluorometric and radioactive tracers (
GALT, Arylsulfatase A, B Glucuronidase, PDH, Fatty acid Oxidation, serum free
fatty acids etc)

Planar Chromatography – TLC for aminoacids and sugars

VLCFAs by GC

Design and operation of a paediatric specific laboratory

Obtaining blood
and fluid samples in small children

Inborn Errors of Metabolism

Genetics:
Principles of Mendelian inheritance, nature and mechanisms of human gene
mutations, genome imprinting

Chromosomal Disorders : Trisomy 21, Fragile X syndrome, Turners, Klinefelters, SRY and Primary sex reversal syndromes

· Disorders of aminoacid and peptide metabolism – Phenylketonuria including the management in pregnancy, homocystinuria, MSUD, Tyrosinaemia, non-ketotic hyperglycinaemia

· Disorders of organic acid metabolism – propionic acidaemia, methylmalonic acidaemia, isovaleric acidaemia, alkaptonuria, glutaric aciduria tye I.

· Hyperammonaemia and urea cycle disorders

· Disorders of carbohydrate metabolism – GSDs, Galactosaemia, small intestinal
disaccharidases, hereditary fructose intolerance)

· Disorders of fatty acid oxidation – Carntine transporter defect, CATR, SCAD,
MCAD, MADD, LCHAD

· Disorders of ketone body metabolism – betaketothiolase deficiency, SCOT

· Lysosomal storage disorders – GSD II Pompes, MPS's, Niemann-Pick, Gauchers, Metachromatic
leukodystrophy, Fabry's, Tay Sachs, Morquios.

· Disorders of lipoproteins and lipid metabolism

· Peroxisomal disorders – peroxisomal biogenesis disorders, refsums, X-ALD, primary hyperoxaluria)

· Disorders of purine metabolism – Lesch-Nyhan and HGPRT, APRT deficiency, ADA and PNP causing
immunodeficiency, myoadenylate deaminase deficiency

· Disorders of calcium metabolism

· Disorders of metal metabolism – Wilson's disease,
Menkes syndrome, hereditary
haemochromatosis)

· Congenital lactic acidosis – mitochondrial respiratory chain disorders, Puruvtae dehydrogenase deficiency, pyruvate carboxylase deficiency

· Porphyrias

· Disorders of cholesterol, sterol and bile acid metabolism

· Disorders of vitamin metabolism – biotin, cobalamin

· Defects of membrane transport – RTA, Cystinuria, Fanconi Syndrome, Hereditary phosphaturic
syndromes, Cystic fibrosis, short QT syndrome lysinuric protein
intolerance, cystinosis, Hartnups

· Defects of glycosylation

· Defects of connective tissue – marfans syndrome

Pediatric Endocrinology

– Thyroid
disorders

– Disorders of
sexual differentiation, Congenital Adrenal Hyperplasia, Androgen insensitivity
syndromes

– Inherited
defects of growth hormone synthesis and action

– Nephrogenic
Diabetes Insipidus

–
Pseudohypoparathyroidism

– Vitamin D and
calcium – rickets

– Type 1 diabetes

– Phaeochromocytoma

– Short Stature

Other Pediatric-specific topics

-Neonatal hyperbilirubinaemia (conjugated and unconjugated)

– Neonatal hypoglycemia

– Rickets

-Nutritional assessment – kwashiorkor and marasmus