

# Paediatric Inherited Metabolic Medicine

Sub-specialty Syllabus

**Version 2**

Approved by the GMC for implementation from 1 September 2021

This document outlines the syllabus to be used by doctors completing Paediatric Inherited Metabolic Medicine training in the United Kingdom (UK). It accompanies the RCPCH Progress curriculum and Assessment Strategy.

This is Version 2.0. As the document is updated, version numbers will be changed and content changes noted in the table below.

Version number	Date issued	Summary of changes
2	September 2021	<p>Document reviewed as part of the Shape of Paediatrics Training review.</p> <p>'Using the Syllabus with ePortfolio' (page 5) updated.</p> <p>Learning Outcome (LO) 7 amended, 'international' replaced with 'multicentre' (page 7).</p> <p>Key Capabilities (KCs) amended and aligned with LOs. Original KC2 moved above of KO1. Original KC1 (now KC2) updated – 'Phenylketonuria' and 'MCAD' removed and added as a separate KC, now KC3, replacement of original KC3.</p> <p>Original KC4 moved, now the new KC6.</p>

This information is correct and up to date at time of publication.  
©RCPCH 2021

# Introduction



This syllabus supports the completion of the RCPCH Progress curriculum and should be used with the curriculum document and Assessment Strategy.

The purpose of the curriculum is to train doctors to acquire a detailed knowledge and understanding of health and illness in babies, children and young people. The curriculum provides a framework for training, articulating the standard required to work at Consultant level, through key progression points during their training, as well as encouraging the pursuit of excellence in all aspects of clinical and wider practice.

The curriculum comprises Learning Outcomes specifying the standard trainees must demonstrate to progress in training and attain a Certificate of Completion of Training (CCT). The syllabi supports the curriculum by providing further instructions and guidance on how the Learning Outcomes can be achieved and demonstrated.

## Using the Syllabus

Paediatric trainees are required to demonstrate achievement of generic and sub-specialty or General Paediatric Learning Outcomes throughout their training period.

For all Level 1 and Level 2 trainees, there are 11 generic paediatric Learning Outcomes for each level. At Level 3, there are a further 11 generic paediatric Learning Outcomes for all trainees and several additional Learning Outcomes in either General Paediatrics or the sub-specialty to which the trainee has been appointed.

This syllabus contains five interlinked elements, as outlined in Figure 1 which illustrates how each element elaborates on the previous one.

## Elements of the Syllabus

The **Introductory Statement** sets the scene for what makes a Metabolic Paediatrician doctor.

The **Learning Outcomes** are stated at the beginning of each section. These are the outcomes which the trainee must demonstrate they have met to be awarded their Certificate of Completion of Training (CCT) in Paediatrics. Progress towards achievement of the Learning Outcomes is reviewed annually at the Annual Review of Competence Progression (ARCP).

Each Learning Outcome is mapped to the GMC (General Medical Council) Generic Professional Capabilities framework. Each trainee must achieve all the Generic Professional Capabilities to meet the minimum regulatory standards for satisfactory completion of training.

The **Key Capabilities** are mandatory capabilities which must be evidenced by the trainee, in their ePortfolio, to meet the Learning Outcome. Key Capabilities are therefore also mapped to the GMC Generic Professional Capabilities framework.

The **Illustrations** are examples of evidence and give the range of clinical contexts that the trainee may use to support their achievement of the Key Capabilities. These are intended to provide a prompt to the trainee and trainer as to how the overall outcomes might be achieved. They are not intended to be exhaustive and excellent trainees may produce a broader portfolio or include evidence that demonstrates deeper learning. It is not expected that trainees provide ePortfolio evidence against every individual illustration (or a set quota); the aim of assessment is to provide evidence against every Key Capability.

The **Assessment Grid** indicates suggested assessment methods, which may be used to demonstrate the Key Capabilities. Trainees may use differing assessment methods to demonstrate each capability (as indicated in each Assessment Grid), but there must be evidence of the trainee having achieved all Key Capabilities.

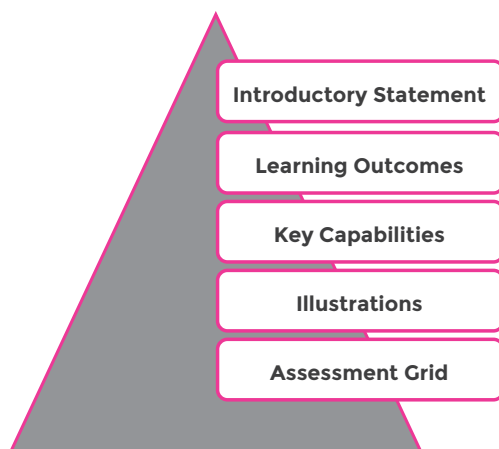


Figure 1: The five elements of the syllabus

## Using the Syllabus with ePortfolio

The ePortfolio is used to demonstrate a trainee's progression using assessments, development logs and reflections. Events should be linked to the Progress curriculum specifically against the key capabilities at the appropriate level.

Further guidance on using the ePortfolio is available on our website: <https://www.rcpch.ac.uk/resources/rcpch-eportfolio-kaizen-guidance-trainees>



# Paediatric Inherited Metabolic Medicine Introductory Statement

---

## Introductory Statement

A Metabolic Paediatrician is a doctor providing care for children, young people and families who have inherited disorders that affect the body's normal biochemical reactions. There are many rare metabolic disorders that can affect the function of any organ system and can present at any age.

They have detailed knowledge of normal human biochemistry and the impact of metabolic diseases and use this knowledge in the diagnostic process (including identifying novel disorders) and in planning management strategies. They strive to improve the early recognition and diagnosis of metabolic diseases, including through newborn screening.

Metabolic Paediatricians work closely with laboratory scientists, metabolic dietitians, pharmacist specialists and nursing teams. They are research-active and keep up to date with the rapid and innovative developments in therapeutics for metabolic disorders. They are advocates for their patients, actively engaging in developing and commissioning high-quality services and evolving therapies.

# Sub-specialty Learning Outcomes

Sub-specialty Learning Outcomes		GMC Generic Professional Capabilities
1.	Recognises, assesses and manages the full range of acute paediatric inherited metabolic emergencies.	GPC 2, 3, 5
2.	Demonstrates sound understanding of the full range of metabolic conditions and applies this knowledge to newly referred patients.	GPC 2, 3, 5
3.	Counsels families of a patient with the diagnosis of an inherited metabolic disorder (IMD) detected through the newborn screening programme.	GPC 1, 2, 3, 4, 5
4.	Explains the inheritance of IMD to families and applies this within a cultural context.	GPC 1, 2, 3, 4, 5
5.	Liaises effectively with hospital and community specialist teams for managing paediatric inherited metabolic conditions, particularly with specialists, such as dietitians, pharmacists, nurses and laboratory scientists.	GPC 1, 2, 3, 4, 5
6.	Effectively works with paediatricians in district general hospitals and specialist centres to coordinate patient care and maintains consistent quality in the context of a paediatric inherited metabolic medicine service.	GPC 1, 2, 3, 4, 5, 6
7.	Contributes to multicentre collaborations and research.	GPC 5, 6, 9

## Key Capabilities

<p>Advises senior colleagues on the investigation and management of a child and young person with the following conditions:</p> <ul style="list-style-type: none"> <li>• KC1.1 - Hyperammonaemia in an acutely unwell child (see Illustration C1 for details)</li> <li>• KC1.2 - Hypoglycaemia</li> <li>• KC1.3 - Cholestasis, liver failure or hepatomegaly/hepatosplenomegaly</li> <li>• KC1.4 - Cardiomyopathy</li> <li>• KC1.5 - Dysmorphic features, corneal clouding/cataracts and/or skeletal dysplasia</li> <li>• KC1.6 - Neurological regression and/or myopathy</li> </ul>	<p>GPC 2, 3, 5, 7</p>
<p>Takes responsibility for the holistic investigation and management of a child and young person with the following conditions:</p> <ul style="list-style-type: none"> <li>• KC2.1 - Branched-chain organic aciduria (see Illustration B1 for details)</li> <li>• KC2.2 - Urea cycle disorder (see Illustration C2 for details)</li> <li>• KC2.3 - Glycogen storage disorder (see Illustration D1 for details)</li> <li>• KC2.4 - Galactosaemia, including dietary management and the early identification of need for educational support (see Illustration D2 for details)</li> <li>• KC2.5 - Long-chain fatty acid oxidation disorder, including dietary management and the management of intercurrent illnesses (see Illustration E2 for details)</li> <li>• KC2.6 - Lysosomal storage disorder (for which there is an approved treatment, see Illustration F1 for details)</li> <li>• KC2.7 - A mitochondrial disorder (see illustration H for details)</li> </ul>	<p>GPC 2, 3, 5, 7</p>
<p>Takes responsibility for the holistic investigation and management of a child and young person with the following conditions:</p> <ul style="list-style-type: none"> <li>• KC3.1 - Phenylketonuria (see Illustration A1 for details).</li> <li>• KC3.2 - Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency, including the counselling of a new family from newborn screening and the management of intercurrent illnesses (see Illustration E1 for details).</li> </ul>	<p>GPC 1, 2, 3</p>
<p>KC4.1 - Understands the available modalities of genetic testing and uses this knowledge to select and consent for the appropriate genetic test for a child or young person with IMD (see illustration J1 for examples).</p> <p>KC4.2 - Understands the ACMG guidelines for variant classification and uses this knowledge to participate in genomic medicine MDTs and discuss the implications of genetic results with families (see illustration J1 for examples).</p>	<p>GPC 1, 2, 3, 5</p>



KC5.1 - Prescribes a range of specialised drugs for the treatment of inherited disorders of metabolism (eg enzyme replacement therapies, ammonia-scavenging medications and other examples given in this syllabus).	GPC 6
KC5.2 - Utilises specialised metabolic investigations, where indicated, with appropriate interpretation and application to the diagnosis of a child or young person with a suspected inherited metabolic disorder (see Illustration K for details).	GPC 3
Undertakes the following procedures: <ul style="list-style-type: none"> <li>• KC5.3 - skin biopsy</li> <li>• KC5.4 - lumbar puncture for neurotransmitter analysis</li> </ul>	GPC 3
KC6.1 - Contributes to effective and up-to-date local and regional multidisciplinary team (MDT) management of children and young people with inherited disorders of metabolism (see Illustration J2 for details).	GPC 2, 3, 5
KC7.1 - Understands the role of clinical trials, natural history studies and registries in the management and development of new treatments for IMD and participates in MDT discussions about study recruitment. KC 7.2 - Contributes to research projects and publications both in their training centre(s) and by collaboration with other centres.	GPC 2, 3, 9

## Illustrations

A Disorders of amino acid metabolism	
Demonstrates a sound knowledge and understanding of the following:	
1.	<p>Phenylketonuria - examples of aspects of management to consider:</p> <ol style="list-style-type: none"> <li>Newborn screening for phenylketonuria - technique, role and counselling for a new diagnosis</li> <li>Effect of hyperphenylalaninaemia on children, young people and foetuses, including management of phenylketonuria in pregnancy</li> <li>Dietary treatment of phenylketonuria, including monitoring and prevention of nutritional deficiencies</li> <li>Drug treatment - sapropterin dihydrochloride (roles and limitations)</li> <li>Testing for and treating the related defects of biopterin metabolism</li> </ol>
2.	<p>Tyrosinaemia - examples of aspects of management to consider:</p> <ol style="list-style-type: none"> <li>Drug treatment - nitisinone (NTBC)</li> <li>Clinical presentations and the long-term complications of tyrosinaemia types 1, 2 and 3</li> <li>Dietary treatment of tyrosinaemia types 1 and 2, including monitoring of a child on dietary treatment/NTBC</li> <li>Indications for liver transplantation in tyrosinaemia type 1</li> </ol>

3.	<p>Homocystinuria - examples of aspects of management to consider:</p> <ol style="list-style-type: none"> <li>Clinical presentation and long-term complications of classical homocystinuria</li> <li>Clinical presentation of remethylation defects</li> <li>Causes of combined homocystinuria and methylmalonic aciduria</li> <li>Drug treatment - betaine and pyridoxine</li> <li>Dietary treatment of homocystinuria, including monitoring of a child or young person on dietary or medical treatment</li> <li>Management and prevention of thromboembolic disease, including pregnancy</li> <li>Pyridoxine responsiveness test</li> <li>Newborn screening for homocystinuria - technique, role and counselling for a new diagnosis</li> </ol>
4.	<p>Maple syrup urine disease (MSUD) - examples of aspects of management to consider:</p> <ol style="list-style-type: none"> <li>Clinical presentations</li> <li>Newborn screening - technique, role and counselling for a new diagnosis</li> <li>Dietary treatment, including monitoring of a child or young person on dietary treatment</li> <li>Management of acute MSUD, including extracorporeal therapy</li> <li>Management of acute illness in a child and young person with MSUD, including the emergency protocol</li> <li>Indications for liver transplantation</li> </ol>
5.	<p>Other aminoacidopathies to consider:</p> <ol style="list-style-type: none"> <li>Hyperornithinaemia with gyrate atrophy, including dietary treatment and complications</li> <li>Alkaptonuria, including the role of NTB</li> </ol>
<b>B Disorders of organic acid metabolism</b>	
Demonstrates a sound knowledge and understanding of the following:	
1.	<p>Branched-chain organic acidurias - examples of aspects of management to consider:</p> <ol style="list-style-type: none"> <li>Propionic acidaemia - clinical presentation</li> <li>Methylmalonic acidaemia - clinical presentation</li> <li>Isovaleric acidaemia - clinical presentation and newborn screening</li> <li>Dietary management of branched-chain organic acidurias, including monitoring</li> <li>Management of intercurrent illness, emergency regimen and decompensation</li> <li>Ensuring adequate nutrition for children with organic acidaemias, including indications for enteral feeding</li> <li>Rarer organic acidurias (eg malonic aciduria)</li> <li>Drug treatment - L-carnitine, carnitine, carnitine, carnitine and vitamin B12 preparations</li> <li>Indications for and arguments for and against organ transplantation in organic acidurias</li> <li>Different managements of biotin/vitamin-responsive organic acidurias, including the vitamin B12 responsiveness test</li> </ol>

2.	<p>Glutaric aciduria - examples of aspects of management to consider:</p> <ol style="list-style-type: none"> <li>a. Clinical presentation of glutaric aciduria type 1</li> <li>b. Newborn screening for glutaric aciduria type 1</li> <li>c. Dietary treatment and monitoring of a child or young person with glutaric aciduria type 1</li> <li>d. Treatment of dystonia in glutaric aciduria type 1 (including the role of deep brain stimulation)</li> <li>e. Management of acute illness in a child or young person with glutaric aciduria type 1, including the emergency regimen</li> <li>f. Different presentations of L- and D-2-hydroxyglutaric aciduria</li> </ol>
<b>C Hyperammonaemia and urea cycle disorders</b>	
Demonstrates a sound knowledge and understanding of the following:	
1.	<p>Acute hyperammonaemia - examples of aspects of management to consider:</p> <ol style="list-style-type: none"> <li>a. Clinical presentation and recognition of hyperammonaemia</li> <li>b. Methods of measuring blood ammonia and the effects of sampling and processing</li> <li>c. Causes of hyperammonaemia, including secondary causes</li> <li>d. Management of acute hyperammonaemia, including extracorporeal treatment</li> </ol>
2.	<p>Urea cycle disorders - examples of aspects of management to consider:</p> <ol style="list-style-type: none"> <li>a. The different presentations of N-Acetyl glutamate synthase (NAGS), Carbamoyl phosphate synthetase (CPS), Ornithine transcarbamylase (OTC), argininosuccinate synthetase (ASS), Argininosuccinate lyase (ASL) and arginase deficiencies</li> <li>b. The different managements and presentations of transport defects, including citrin deficiency, lysinuric protein intolerance and Hyperornithinemia-hyperammonemia-homocitrullinuria (HHH)</li> <li>c. Dietary management of urea cycle disorders, including monitoring</li> <li>d. Emergency regimens for and management of intercurrent illness/ decompensations</li> <li>e. Ensuring adequate nutrition for children with urea cycle disorders, including indications for enteral feeding</li> <li>f. Drug treatment - carnitine, sodium benzoate, sodium/ glycerol phenylbutyrate, citrulline and L-arginine</li> <li>g. Indications for organ transplantation in urea cycle disorders</li> </ol>

## D Disorders of carbohydrate metabolism

Demonstrates a sound knowledge and understanding of the following:

1. Glycogen storage diseases (GSDs) – examples of aspects of management to consider:
  - a. Different presentations of GSD 1a and 1b, including the management of neutropenia and inflammatory bowel disease
  - b. Different presentations of GSD III, IV, VI and IX
  - c. Different presentations of muscle GSDs, including GSD V, VII and IX
  - d. Monitoring of a child or young person on dietary treatment for GSD, including the use of glucose–lactate profiles and continuous glucose monitoring
  - e. Dietary treatment of GSDs associated with fasting intolerance, including the use of corn starch and enteral feedings
  - f. Management of intercurrent illness and emergency regimens
  - g. Indications for liver transplantation in GSD
2. Galactosaemia – examples of aspects of management to consider:
  - a. Clinical presentation of classical galactosaemia and the differential diagnosis of neonatal liver failure
  - b. Long-term complications, including learning difficulties and referral for educational support
  - c. Recognition and management of ovarian failure in females
  - d. Dietary treatment of galactosaemia and monitoring
  - e. Molecular and enzymatic investigations of galactosaemia, including Duarte variants
3. Other rare carbohydrate metabolism disorders – examples of conditions to consider:
  - a. Fructosaemia
  - b. Fructose 1,6-bisphosphatase deficiency
  - c. Glucose transporter deficiency (GLUT1), including the use of the ketogenic diet
  - d. Fanconi-Bickel syndrome

## E Disorders of fatty acid oxidation and ketone body metabolism

Demonstrates a sound knowledge and understanding of the following:

1. MCAD deficiency (MCADD):
  - a. Newborn screening for MCADD - technique, role and counselling for a new diagnosis
  - b. Dietary treatment of MCADD, including emergency regimens and appropriate fasting tolerances in infancy
2. Long-chain fatty acid oxidation disorders:
  - a. The different presentations of Very long-chain acyl-CoA dehydrogenase deficiency (VLCAD deficiency), Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency and mitochondrial Trifunctional protein deficiency (TFP) deficiency
  - b. The different presentations of disorders of carnitine transport - Carnitine palmitoyltransferase I (CPT1), Carnitine palmitoyltransferase 2 (CPT2), Carnitine-acylcarnitine translocase (CACT) and carnitine transporter deficiencies
  - c. Dietary treatment for a child or young person with a long-chain fatty acid oxidation disorder, including monitoring
  - d. Management and investigation of metabolic causes of rhabdomyolysis
  - e. Management of intercurrent illness and emergency regimens in fatty acid oxidation disorders
3. Other disorders of fatty acid oxidation and ketone body metabolism:
  - a. The different presentations and management of glutaric aciduria type 2 and Multiple Acyl-CoA-Dehydrogenase Deficiency (MADD)
  - b. Drug treatment - riboflavin for some cases of MADD
  - c. The different presentations and management of Short-chain acyl-CoA dehydrogenase (SCAD) and Short chain 3-hydroxyacyl-CoA dehydrogenase (SCHAD) deficiencies
  - d. The different presentations and management of ketolytic defects, eg Methionine adenosyl transferase (MAT) and Succinyl-CoA:3-oxoacid CoA transferase (SCOT) deficiencies
  - e. The different presentations and management of ketogenic defects (eg HMG CoA synthase and lyase deficiencies)

## F Lysosomal storage disorders

Demonstrates a sound knowledge and understanding of the following:

1. Lysosomal storage disorders (LSDs) for which there is an approved therapy - examples of aspects of management to consider:
  - a. The different clinical presentations and treatments for the mucopolysaccharidoses (I, II, IV and VI)
  - b. The different clinical presentations and treatments for Fabry disease, Gaucher disease (I and III), Pompe disease, Danon disease and lysosomal acid lipase deficiency
  - c. The different clinical presentations and treatments for Niemann-Pick disease type C
  - d. Drug treatments - laronidase, idursulfase, elosulfase alfa, galsulfase, agalsidase alfa/beta, imiglucerase, velaglucerase, alglucosidase alfa, sebelipase alfa, miglustat and migalastat
  - e. Monitoring of children and young people on enzyme replacement or substrate reduction, including awareness of agreed protocols for treatment monitoring and continuation
  - f. Management of drug-associated reactions and side effects of approved treatments for LSDs
  - g. Understanding of the indications for choice and complications of central venous catheters for enzyme replacement
  - h. Understanding of anaesthetic and surgical considerations for children with MPS disorders
  - i. Indications for stem-cell transplantation for some LSDs
2. LSDs for which there is no approved therapy - examples of aspects of management to consider:
  - a. The different clinical presentations of Krabbe disease, metachromatic leukodystrophy and multiple sulfatase deficiency
  - b. The different clinical presentations of Niemann-Pick diseases (types A and B) and the mucopolysaccharidoses (III, VII and IX)
  - c. The different clinical presentations of GM1 and GM2 gangliosidoses, mannosidosis and other oligosaccharidosis
  - d. Familiarity with the current state of clinical trials of novel therapies for currently untreatable LSDs
  - e. Indications for stem-cell transplantation for some otherwise untreatable LSDs
  - f. Understanding of effective palliative care for degenerative diseases

## G Disorders of lipid metabolism

Demonstrates a sound knowledge and understanding of the following:

1. Familial hypercholesterolaemia (FH) - examples of aspects of management to consider:
  - a. Diagnostic criteria and clinical signs of FH
  - b. Drug treatment - indications, side effects and monitoring of cholesterol-lowering medications
  - c. Dietary recommendations for FH
  - d. Assessment of cardiovascular risk in patients with hypercholesterolaemia
  - e. Treatments available for homozygous FH, including referral for liver transplantation
2. Rare disorders of lipid metabolism - examples of aspects of management to consider:
  - a. Clinical presentation and dietary treatment of lipoprotein lipase deficiency
  - b. Disorders of cholesterol synthesis, including Smith-Lemli-Opitz syndrome and the use of cholesterol supplementation
  - c. Clinical presentation and treatments of abetalipoproteinaemia and hypobetalipoproteinaemia

## H Mitochondrial disorders (may include a period of training in neurology)

Demonstrates a sound knowledge and understanding of the following:

1. Mitochondrial disease - aspects of management to consider:
  - a. The differing clinical presentations and long-term complications of Leigh syndrome, Mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELAS), Myoclonic epilepsy with ragged red fibres (MERRF), Neuropathy, ataxia and retinitis pigmentosa (NARP), Leber's hereditary optic neuropathy (LHON), Pearson syndrome, Kearns-Sayre syndrome, Mitochondrial neurogastrointestinal encephalopathy syndrome (MNGIE) syndrome, Barth syndrome, ethylmalonic encephalopathy
  - b. The different clinical presentations of disorders associated with mitochondrial DNA depletion, including Alpers' syndrome
  - c. The different clinical presentations and long-term complications of pyruvate dehydrogenase deficiency and pyruvate carboxylase deficiency
  - d. Drug treatment - indications for and limitations of ubiquinone, biotin, riboflavin, thiamine and sodium dichloroacetate
  - e. Advising appropriate investigations for an undiagnosed child with primary lactic acidosis, including diagnostic tissue biopsies
  - f. Understanding of effective palliative care for degenerative diseases

## I Neurometabolic and other disorders (may include a period of training in neurology)

Demonstrates a sound knowledge and understanding of the following:

1. Neonatal seizures - examples of conditions and aspects of management to consider:
  - a. Nonketotic hyperglycinaemia
  - b. Pyridoxine- and pyridoxal phosphate-dependent epilepsies
  - c. Disorders of serine metabolism
  - d. Disorders of purine metabolism, including sulphite oxidase deficiency and molybdenum cofactor deficiency
  - e. Disorders of metal metabolism, including Menkes disease and Wilson's disease
  - f. Drug treatments - indications and limitations of pyridoxine, pyridoxal phosphate, copper histidine injections, dextromethorphan, serine, zinc, penicillamine, trientine and cyclic PMP
2. Other neurometabolic disorders - examples of conditions and aspects of management to consider:
  - a. Disorders of peroxisomal biogenesis
  - b. Single enzyme disorders of peroxisomal metabolism, including X-linked adrenoleukodystrophy
  - c. Disorders of purine metabolism, including Lesch-Nyhan syndrome
  - d. Disorders of pyrimidine metabolism
  - e. Disorders of neurotransmission
  - f. Cerebral folate and creatine deficiency syndromes
  - g. The different clinical presentations of, investigations for and management of the porphyrias, including the treatment of acute intermittent porphyria with haem arginate
  - h. Drug treatments - indications for and limitations of drugs for neurometabolic disease (eg L-dopa, folinic acid, 5-hydroxytryptophan, dextromethorphan and haem arginate)
  - i. Management of X-linked adrenoleukodystrophy, including an awareness of Lorenzo's Oil and the indications for stem-cell transplantation
3. Other disorders - examples of conditions and aspects of management to consider:
  - a. The different clinical presentations of and diagnostic protocols for the congenital disorders of glycosylation
  - b. The presentation, investigation and management of trimethylaminuria



## J Genetics and generic skills (may include a period of training within clinical genetics)

Demonstrates a sound knowledge and understanding of the following:

1. Genetic testing and counselling – examples of aspects to consider:
  - a. Understanding and ability to explain simply the principles of autosomal recessive, dominant, X-linked and mitochondrial DNA inheritance patterns
  - b. Understanding and ability to explain simply the principles of DNA mutation analysis and sequencing
  - c. Understanding and ability to explain simply the different ways of performing antenatal or prenatal / preimplantation / presymptomatic genetic diagnosis and understanding of the cultural differences in attitudes towards these
  - d. Familiarity with clinical situations in which molecular testing may be an appropriate first-line investigation and the selection of appropriate samples for testing (eg genomic DNA vs cDNA)
  - e. Understanding issues regarding informed consent for DNA testing and whole exome or genome testing
  - f. Understand the available modalities of genetic testing (single gene/variant, gene panel, exome, genome)
2. Maintaining standards in inherited metabolic disorders – examples of aspects to consider:
  - a. Knowledge of external quality assurance schemes for laboratories
  - b. Critical appraisal of published literature, including a working knowledge of medical statistics
  - c. How to use online resources, such as Online Mendelian Inheritance in Man (OMIM) to obtain up-to-date information on inherited metabolic disorders
  - d. Participation in and keeping up to date with multicentre research studies of inherited metabolic disorders

## K Technical skills

Conducts:

1. Metabolic investigations – examples to be familiar with:
  - a. Acylcarnitines
  - b. Urine organic acids, including Gas chromatography/mass spectrometry (GC/MS) data
  - c. Quantitative amino acid profiles
  - d. Enzyme assays
  - e. Urinary glycosaminoglycan and oligosaccharide analysis
  - f. Urine purine and pyrimidine data
  - g. Lipid profiles/lipoprotein electrophoresis
  - h. Plasma very long-chain fatty acids (and other investigations for peroxisomal disease)
  - i. Molecular genetic analyses
2. Dynamic tests – examples to be familiar with:
  - a. Allopurinol loading test
  - b. Penicillamine challenge
  - c. Responsiveness tests to pyridoxine/pyridoxal phosphate and vitamin B12

3. Invasive investigations - examples to perform/recommend and/or interpret include:
  - a. Muscle biopsy for respiratory chain analysis (recommend)
  - b. Liver biopsy for enzymology (recommend)
  - c. Skin biopsy for fibroblast culture and enzymology
  - d. Lumbar puncture for CSF neurotransmitters, glucose, catecholamines and amino acids
  - e. Awareness of specific counselling for peri- and post-mortem sampling

# Assessment Grid

This table suggests assessment tools which may be used to assess the Key Capabilities for these Learning Outcomes. This is not an exhaustive list and trainees are permitted to use other methods within the RCPCH Assessment Strategy to demonstrate achievement of the Learning Outcome, where they can demonstrate these are suitable.

Key Capabilities	Assessment / Supervised Learning Event suggestions										
	Paediatric Mini Clinical Evaluation (ePaed Mini-CEX)	Paediatric Case-based Discussion (ePaed Cbd)	Paediatric Case-based Discussion (ePaed Cbd)	Directly Observed Procedure / Assessment of Performance (DOP/Aop)	Acute Care Assessment Tool (ACAT)	Discussion of Correspondence (DOC)	Clinical Leadership Assessment Skills (LEADER)	Handover Assessment Tool (HAT)	Paediatric Multi Source Feedback (ePaed MSF)	Paediatric Carers for Children Feedback (Paed CCF)	Other
<p>Advises senior colleagues on the investigation and management of a child and young person with the following conditions:</p> <ul style="list-style-type: none"> <li>Hyperammonaemia in an acutely unwell child (see Illustration C1 for details).</li> <li>Hypoglycaemia.</li> <li>Cholestasis, liver failure or hepatomegaly/hepatosplenomegaly.</li> <li>Cardiomyopathy.</li> <li>Dysmorphic features, corneal clouding/cataracts and/or skeletal dysplasia.</li> <li>Neurological regression and/or myopathy</li> </ul>	✓	✓				✓	✓	✓			
<p>Takes responsibility for the holistic investigation and management of a child and young person with the following conditions:</p> <ul style="list-style-type: none"> <li>Branched-chain organic aciduria (see Illustration B1 for details)</li> <li>Urea cycle disorder (see Illustration C2 for details)</li> <li>Glycogen storage disorder (see Illustration D1 for details)</li> <li>Galactosaemia, including dietary management and the early identification of need for educational support (see Illustration D2 for details)</li> <li>Long-chain fatty acid oxidation disorder, including dietary management and the management of intercurrent illnesses (see Illustration E2 for details)</li> <li>Lysosomal storage disorder (for which there is an approved treatment, see illustration F1 for details)</li> <li>A mitochondrial disorder (see illustration H for details)</li> </ul>	✓	✓				✓	✓	✓			

Key Capabilities	Assessment / Supervised Learning Event suggestions									
	Paediatric Mini Clinical Evaluation (ePaed Mini-CEX)	Paediatric Case-based Discussion (ePaed Cbd)	Directly Observed Procedure / Assessment of Performance (DOP/AoP)	Acute Care Assessment Tool (ACAT)	Discussion of Correspondence (DOC)	Clinical Leadership Assessment Skills (LEADER)	Handover Assessment Tool (HAT)	Paediatric Multi Source Feedback (ePaed MSF)	Paediatric Carers for Children Feedback (Paed CCF)	Other
Takes responsibility for the holistic investigation and management of a child and young person with the following conditions: <ul style="list-style-type: none"> <li>Phenylketonuria (see Illustration A1 for details)</li> <li>Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency, including the counselling of a new family from newborn screening and the management of intercurrent illnesses (see Illustration E1 for details)</li> </ul>	✓	✓			✓			✓		
Understands the available modalities of genetic testing and uses this knowledge to select and consent for the appropriate genetic test for a child or young person with IMD (see illustration J1 for examples).		✓			✓	✓		✓		
Understands the ACMG guidelines for variant classification and uses this knowledge to participate in genomic medicine MDTs and discuss the implications of genetic results with families (see illustration J1 for examples)		✓			✓	✓		✓		
Prescribes a range of specialised drugs for the treatment of inherited disorders of metabolism (eg enzyme replacement therapies, ammonia-scavenging medications and other examples given in this syllabus).	✓	✓	✓					✓		
Utilises specialised metabolic investigations, where indicated, with appropriate interpretation and application to the diagnosis of a child or young person with a suspected inherited metabolic disorder (see Illustration K for details).	✓	✓						✓		
Undertakes the following procedures: <ul style="list-style-type: none"> <li>skin biopsy</li> <li>lumbar puncture for neurotransmitter analysis</li> </ul>	✓	✓	✓					✓		
Contributes to effective and up-to-date local and regional multidisciplinary team (MDT) management of children and young people with inherited disorders of metabolism (see Illustration J2 for details).		✓			✓	✓		✓		
Understands the role of clinical trials, natural history studies and registries in the management and development of new treatments for IMD and participates in MDT discussions about study recruitment.										
Contributes to research projects and publications both in their training centre(s) and by collaboration with other centres.										

