The Paediatric Perspective of Inborn Errors of Metabolism in Hong Kong

RKN **Yuen**
Department of Paediatrics, Kwong Wah Hospital

Inborn errors of metabolism (IEM) are disorders caused by a deficiency of enzyme catalysis or an enzyme that facilitates the transport of biological substances across membranes. More than 500 inherited metabolic diseases have been identified so far. Although individually rare, inborn errors of metabolism are relatively common collectively and early diagnosis and treatment may reverse acute symptoms and prevent chronic damage. Accurate diagnosis can help in future family planning, genetic counselling and prenatal diagnosis.

Chinese children with glycogen storage disease, Gaucher disease and galactosemia were first reported in Hong Kong in 1966. Since then, homocystinuria, hereditary fructose intolerance, mitochondrial disease, Leigh's disease, methymalonic acidaemia, maple syrup urine disease and urea cycle defect have been reported in Chinese children in Hong Kong.

Some children with inborn errors of metabolism present in the neonatal period. Clinical clues to IEM in neonate include unexplained deterioration in an infant well at birth, persistent vomiting with no anatomical cause, major organ failure e.g. liver, heart, encephalopathy, intractable convulsion and congenital anomalies e.g. cataract. Metabolic conditions such as mucopolysaccharidosis, Gaucher disease, mucolipidosis, mitochondrial disease and glycogen storage disease can present as hydrop foetalis in newborn. History of consanguious marriage, recurrent abortion, unexplained neonatal death and positive family history are suggestive of the diagnosis of inherited metabolic disease in neonates. First line investigations for IEM include full blood count, urea, electrolytes, glucose, blood gas, anion gap, ammonia, fasting lactate, pyruvate, liver functions tests, uric acid and urine for reducing substance, ketones and sulphite. Second line investigations such as urine for organic acid and orotic acid, plasma and urea for amino acid pattern, plasma carnitine and acylcarnitine profile and CSF lactate, glycine and amino acid should be considered in selected cases. Third line investigations include enzyme assay on skin fibroblast or blood cell, DNA mutation analysis and special metabolic studies e.g. very long chain fatty acid profile are required to confirm suspected cases.

With the support of hospital paediatricians of regional public hospitals, a Hong Kong Paediatric Metabolic Registry was set up in 2002. Over 40 patients with lysosomal diseases e.g. mucopolysaccharidosis, oligosaccharidosis, sphingolipidosis, mucolipidosis and gangliosidosis have been registered. Over thirty patients with organic acidaemia including glutaric aciduria type l, methymalonic aciduria, multiple carboxylase deficiency, propionic aciduria have been seen. Disorders in carbohydrate metabolism including glycogen storage disease, galactosaemia and fructose intolerance were diagnosed in over thirty patients. Mitochondrial disease including mitochondrial encephalomyopathy, lactic acidosis and stroke-like episodes (MELA) was diagnosed in over twenty patients. Amino acid disorders such as cystinuria, tyrosinaemia, maple syrup urine disease, phenyketonuria, non-ketotic hyperglycinaemia, homocystinuria have been diagnosed as well. The diagnosis of fatty acid oxidation disorders including carnitine cycle defect, multiple acyl-CoA dehyrogenase deficiency was made in nearly twenty children. Urea cycle disorders was diagnosed in 17 children. Perixisomal disorders namely X-linked adrenoleukodystropy and Zellweger syndrome were diagnosed in over ten patients.