New Zealand Paediatric Surveillance Unit
INBORN ERRORS OF METABOLISM

Objectives: To determine the incidence of inborn errors of metabolism in New Zealand.
To describe how these diagnoses are currently made and at what age.
To determine the severity of presenting illness and sequelae of these conditions.
To reassess these factors after the proposed introduction of expanded newborn screening (if this occurs).

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Background:

Inborn errors of metabolism detectable through newborn screening can be divided into four broad categories. These are:

1) **Amino acid disorders** – recognised by elevation of the characteristic amino acid. The most common of these is phenylketonuria (PKU).
2) **Organic acidaemias** – caused by accumulation of toxic organic acids and typically resulting in severe, recurrent metabolic acidosis and ketonuria with other variable biochemical derangements. Examples include propionic acidaemia and methylmalonic acidaemia.
3) **Urea cycle defects** – prevent the elimination of waste nitrogen from protein catabolism, resulting in hyperammonaemia and elevation of precursor amino acids in some cases. Symptoms include lethargy, poor feeding, and vomiting and lead rapidly to coma, cerebral oedema and death. Examples include ornithine transcarbamylase deficiency (OTC) and citrullinaemia
4) **Fatty acid oxidation defects** – due to enzyme deficiencies in the oxidation of fatty acids to ketones and glucose. Typical features are hypoketotic hypoglycaemia and hepatic encephalopathy. Medium chain acyl CoA dehydrogenase deficiency (MCAD) is the most common of these.

Tandem Mass Spectrometry

A new laboratory technique, tandem mass spectrometry (MS/MS) allows about 30 inborn errors of metabolism to be diagnosed from the Guthrie card. This type of screening has already been introduced in many parts of the world including several Australian states, and may also be introduced in New Zealand. Therefore the aim of this study is to more precisely define the epidemiology of inborn errors of metabolism in New Zealand and to monitor the impact of expanded newborn screening if it is introduced.

Case Definition and Reporting Instructions

Please report any new patient seen in the last month, less than 16 years of age with an INBORN ERROR OF METABOLISM (urea cycle, amino acid, organic acid disorder or fatty acid oxidation defect, please refer to complete list of disorders attached if in any doubt). Includes those diagnosed through Neonatal Screening.

Follow-up of positive returns:

A short questionnaire requesting demographic and clinical details will be forwarded to respondents reporting a case. A follow up questionnaire will be sent out at a later date.

Complete List of Disorders

Urea cycle

Carbamyl phosphate synthetase deficiency
Ornithine transcarbamylase deficiency
Arginosuccinate synthase deficiency
Arginosuccinate lyase deficiency
Arginase deficiency
Citrullinemia type 2 (citrin deficiency)

Fatty Acid

Short chain acyl CoA dehydrogenase deficiency
Medium chain acyl CoA dehydrogenase deficiency
Very long chain acyl CoA dehydrogenase deficiency
Long chain 3 hydroxyacyl CoA dehydrogenase deficiency
Multiple acyl CoA dehydrogenase deficiency
Carnitine transporter defect
Carnitine palmitoyl transferase deficiency (types 1 and 2)
Carnitine acylcarnitine translocase deficiency

Organic acid

Propionyl CoA carboxylase deficiency
Methylmalonyl CoA mutase deficiency
Cobalamin C defect
Isovalericacidemia
Glutaryl CoA dehydrogenase deficiency
Holocarboxylase synthase deficiency
Biotinidase deficiency
Hydroxymethylglutaryl CoA lyase deficiency
Methylglutaconicaciduria
3 Methylcrotonyl CoA carboxylase deficiency
3 Ketothiolase deficiency

Amino acid

Phenylketonuria
Glycine encephalopathy (previously known as nonketotic hyperglycinaemia)
Homocystinuria
Maple syrup urine disease
Tyrosinaemia (types 1 and 2)

THANK YOU FOR YOUR HELP AND SUPPORT
THE RESULTS OF THIS SURVEILLANCE WILL BE INCLUDED IN THE ANNUAL REPORT OF THE NZPSU WHICH WILL BE SENT TO ALL PARTICIPATING CLINICIANS