Screening for Fatty Acid Oxidation Disorders
Newborn Metabolic Screening Programme

Introduction The Newborn Metabolic Screening Programme (NMSP) added screening for fatty acid oxidation disorders to the panel of tested disorders in December 2006 with the introduction of expanded newborn screening.

These conditions are genetic metabolic disorders (inborn errors of metabolism) which occur in the breakdown (oxidation) of fatty acids into energy. Energy for the body is obtained firstly from recently eaten food, then from glycogen stored in the liver and lastly from stored fat (fatty acids). If one of the enzymes which break down fatty acids is missing or not working correctly, the person will have a fatty acid oxidation disorder (FAOD). The most common FAOD is MCAD (medium-chain acyl-CoA dehydrogenase deficiency). FAODs are named according to the length of fatty acid chain that can't be broken down or the missing vitamin cofactor. It is thought six to eight babies with a FAOD will be detected through the screening programme each year.

Why screen? FAODs typically present in infancy or early childhood when there is an inter-current illness or another reason why the baby does not feed normally. When the dietary and liver sources of energy are exhausted these babies who cannot break down fat can get dangerously low blood glucose and may become comatose or die. There can be long-term effects of the coma. If it is known that the baby has a FAOD, care can be taken to ensure baby does not fast too long, especially during times of normal childhood illnesses, and if necessary energy, usually in the form of simple carbohydrates, can by given by naso-gastric or venous means. Knowledge of the presence of a FAOD dramatically reduces the morbidity and mortality from the disorders.

These conditions are inherited in an autosomal recessive way which means that sometimes babies detected through the screening programme have older siblings also affected. Some of these older children found since screening started in New Zealand have already had hospital admissions for hypoglycaemia but the cause was not found. Hence screening can benefit other family members as well as the baby.

We have shown that these conditions are not well detected by waiting for baby to become ill and then doing diagnostic testing.[1]

How is baby screened? The testing uses the same blood spot collected for PKU and other screening. This heel prick blood is collected at 48 hours or as soon as possible after this. A baby of this age will have lost a significant proportion of body weight after birth, often by metabolising body fat and the products of this (acylcarnitines) can be measured with a tandem mass spectrometer. Different acylcarnitines indicate different FAODs.

What happens after a positive screen? Positive screening tests come in two levels, like other tests from the programme.

1. If the results strongly suggest a disorder is present the result will be phoned to the lead maternity carer (LMC). The phone call will be made by a metabolic physician or senior screening programme staff. They will ask about the baby and be able to advise on immediate treatment should this be appropriate. A second dried blood spot and urine will be required to confirm the diagnosis.

2. Where the results are abnormal, but not highly suggestive that a condition is present, a letter to the LMC will ask for a second blood sample.

What is the treatment? Children with FAODs are mostly well. Treatment can be as simple as family advice about feeding. In some cases special foods or additional vitamins may be required. Children from the Auckland area will be cared for by the metabolic team (Dr Callum Wilson, physician; Ms Rhonda Akroyd, dietician; and Ms Christine McMahon, nurse). From the rest of New Zealand care will mostly be from a local paediatrician, generally consulting with the metabolic team.

Which FAODs can be found by screening? In New Zealand we are able to detect the following disorders by measuring acylcarnitine levels.

- CACT (carnitine acylcarnitine translocase deficiency)
- Carnitine transporter defect
- CPT-I (carnitine palmitoyltransferase-I deficiency)
- CPT-II (carnitine palmitoyltransferase-II deficiency)
- LCHAD (3-hydroxy long-chain acyl-CoA dehydrogenase deficiency
- TFP (trifunctional protein deficiency)
- MADD (multiple acyl-CoA dehydrogenase deficiency)
- MCAD (medium-chain acyl-CoA dehydrogenase deficiency)
- VLCAD (very-long-chain acyl-CoA dehydrogenase deficiency).

1. *Wilson, C., et al., The failure to diagnose inborn errors of metabolism in New Zealand: the case for expanded newborn screening. New Zealand Medical Journal, 2007.* ***120****(1262): p. e-pub.*