Alberta Health Services
Newborn Metabolic Screening

Information for Health Professionals

Tri-Functional Protein (TFP) Deficiency

(metabolic condition: fatty acid oxidation disorder)

Also known as:

- mitochondrial trifunctional protein deficiency
- trifunctional enzyme deficiency
- type 2 trifunctional protein deficiency

What are fatty acid oxidation disorders?

Fatty acid oxidation disorders (FAOD) are a group of inherited conditions in which fatty acids cannot be broken down to provide the body with energy. Fatty acids are a key source of energy during fasting or stress, such as during an illness. An inability to metabolize fatty acids leads to an accumulation of toxic metabolites in the body along with cellular energy deficiency which in combination can cause serious health problems.

What is TFP deficiency?

Tri-functional protein (TFP) is a mitochondrial protein with three different enzyme activities necessary for the breakdown of fatty acids to produce energy. One of these enzymes is long chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD). TFP breaks down fatty acids 10 carbon atoms in length and longer. People with TFP deficiency are unable to break down these long chain fatty acids to produce energy.

What causes TFP deficiency?

Several different mutations in the TFP gene cause absent or decreased activity of all three enzymes in the TFP protein. Other mutations affect only LCHAD activity while the remaining two enzymes have normal activity.

How common is TFP deficiency?

TFP deficiency is a rare condition; the incidence is unknown.

What are the clinical features of TFP deficiency?

Although infants with TFP deficiency may appear normal at birth, during a period of fasting (such as during a common illness), a child who was previously healthy may present with irritability, lethargy, vomiting or diarrhea, hypotonia, hypoketotic hypoglycemia, and seizures. Muscle weakness may lead to the development of breathing problems. This can progress quickly to coma and death if treatment is not started quickly. These children may also have developmental delay, poor weight gain, cardiomyopathy and liver problems. Periods of heavy exercise can also trigger episodes. The presentation of TFP deficiency is variable and there may be individuals with the disorder who have a milder course with onset in childhood or adulthood.

What is the screening test for TFP deficiency?

A specific pattern of fatty acid metabolites is detected on the newborn blood spot screen. Newborn blood spot screening is not 100% perfect. Infants with clinical symptoms need timely assessment and diagnostic testing even if their screen result is normal.

How is the diagnosis confirmed?

The diagnosis of TFP deficiency is confirmed by detecting specific metabolites in urine or on blood acylcarnitine analysis. Further testing may include enzyme analysis and/or mutation analysis of the TFP gene. In order to distinguish LCHAD deficiency from TFP deficiency, further diagnostic testing is required. Specialists at the clinics listed below will arrange diagnostic testing.

How is TFP deficiency treated?

TFP deficiency is treated by avoidance of fasting. Carnitine supplementation together with a diet which is low in long chain fatty acids may be considered. Parent education is an important component of treatment, including advising parents on actions to be taken when their child develops a minor illness. Prompt treatment of a metabolic crisis with intravenous fluids and glucose is necessary. The treatment is lifelong.

What is the outcome of treatment for TFP deficiency?

Effective treatment can prevent metabolic crises and improve the outcome of this disorder.

Is TFP deficiency inherited?

TFP deficiency is inherited as an autosomal recessive trait. Parents of a child with TFP deficiency are carriers of the condition and have a 1 in 4 chance of having another affected child in each subsequent pregnancy. TFP deficiency carriers are healthy. Genetic counselling and prenatal testing is available to all families with TFP deficiency.

For additional resources, please call:

Clinical & Metabolic Genetics Program (Edmonton)

8-53 Medical Sciences Building
8440 – 112 St. NW
Edmonton, AB T6G 2H7
Phone: 780-407-7333
Fax: 780-407-6845

Emergency consultations:
Phone 780-407-8822 and ask for the specialist on call for metabolic diseases.

Clinical & Metabolic Genetics Program (Calgary)

Alberta Children's Hospital
28 Oki Drive NW
Calgary, AB T3B 6A8
Phone: 403-955-7587
Fax: 403-955-3091

Emergency consultations:
Phone 403-955-7211 and ask for the specialist on call for metabolic diseases.

Early screening, detection and treatment – every infant, every time

For more information about the NMS Program, visit www.ahs.ca/newbornscreening

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