

Long Chain 3-Hydroxyacyl-CoA Dehydrogenase (LCHAD) & Tri-Functional Protein (TFP) Deficiency

(metabolic condition: fatty acid oxidation disorders) *Information for Health Professionals*

Also known as:

LCHAD

- long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency
- long-chain 3-OH acyl-CoA dehydrogenase deficiency
- type 1 trifunctional protein deficiency

TFP

- mitochondrial trifunctional 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 are LCHAD and TFP deficiency?

Newborn screening cannot distinguish LCHAD and TFP deficiency therefore the screen result is reported as critical for both conditions. LCHAD and TFP deficiency occur when the tri-functional protein does not work correctly and the body is therefore unable to break down long chain fatty acids to produce energy.

What causes LCHAD and TFP deficiency?

Tri-functional protein is formed by two subunits encoded by the HADA and HADB genes. Pathogenic variants in either gene completely abolish the protein's function and cause TFP deficiency. Specific variants in the HADA gene cause LCHAD deficiency.

How common are LCHAD and TFP deficiency?

LCHAD and TFP deficiency are rare conditions; the incidence is unknown.

What are the clinical features of LCHAD and TFP deficiency?

Although infants with LCHAD deficiency may appear normal at birth, during a period of fasting (such as during a common illness), an infant who was previously healthy may present with lethargy, vomiting or diarrhea, hypoketotic hypoglycemia, hypotonia, and seizures. This can progress quickly to coma and death. These children may also have developmental delay, poor weight gain, neurological problems, liver disease and cardiomyopathy. The first episode usually occurs in infancy or early childhood.

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 LCHAD and TFP deficiency?

A specific pattern of fatty acid metabolites is detected on the newborn blood spot screen. Newborn blood spot screening will not detect all infants with LCHAD and TFP deficiency. Infants with clinical symptoms need timely assessment and diagnostic testing even if their screen result is normal.

How is the diagnosis confirmed?

In order to distinguish LCHAD deficiency from TFP deficiency, further diagnostic testing is required. The diagnosis of LCHAD and TFP deficiency is confirmed by detecting specific metabolites in urine or on blood acylcarnitine analysis. Further testing may include enzyme analysis and/or molecular genetic analysis. The Clinical Metabolic Genetics Program will arrange diagnostic testing.

How are LCHAD and TFP deficiency treated?

LCHAD and TFP deficiency are treated by avoidance of fasting. Carnitine supplementation together with a diet which is low in long chain fatty acids may be considered. Prompt treatment of a metabolic crisis with intravenous fluids and glucose is necessary to prevent neurological problems. Treatment can be effective in preventing metabolic crises and their sequelae. The treatment is lifelong.

Continued on next page >

Early screening and follow-up care – every baby, every time

For more information about the Alberta Newborn Screening Program, visit www.ahs.ca/newbornscreening

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Are LCHAD and TFP deficiency inherited?

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

Additional resources are available through:

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.

