Long Chain 3-hydroxyacyl-CoA Dehydrogenase (LCHAD) Deficiency
Information for Healthcare Professionals

Long chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency is caused by an enzyme defect in the mitochondrial beta-oxidation cycle. This results in an inability of the body to break down long fatty acids into a usable energy source (ketones). Unrecognized, LCHAD deficiency may be rapidly progressive and fatal secondary to its cardiac involvement. It is classified as a fatty acid oxidation disorder.

✓ Clinical Symptoms

LCHADD can cause mild effects in some people and more serious health issues in others. Babies and children usually begin to have symptoms sometime from birth through age two. LCHAD deficiency causes episodes of hypoglycemia. This can include fatigue, hypotonia, nausea, vomiting, irritability, and behavior changes. If hypoglycemia is not treated, a child with LCHAD deficiency can develop respiratory problems, swelling of the brain, seizures and coma.

Symptoms often happen after fasting for more than a few hours. Symptoms are also more likely to occur when children get sick or have an infection. Between episodes of hypoglycemia, people with LCHAD deficiency are usually healthy; however, repeated episodes can cause brain damage. This can result in learning disabilities or intellectual disabilities.

Babies and children who are not treated may have poor weight gain, delays in learning, delays in walking and other motor skills, enlarged liver and other liver problems, enlarged heart and other heart problems, and vision loss due to build-up of pigment in the retina.

Some children with LCHADD have never had symptoms and are only found to be affected after a brother or sister is diagnosed.

Mothers of babies with LCHAD deficiency may have problems during pregnancy. These problems may include anorexia, vomiting, abdominal pain, and jaundice during the third trimester of pregnancy. If untreated, it can cause HELLP syndrome or acute fatty liver of pregnancy (AFLP) and possibly the need for a liver transplant or even death. Less frequently, pregnancies with babies affected with other fatty acid oxidation disorders may be complicated by HELLP syndrome or AFLP.

✓ Incidence

LCHAD deficiency occurs in greater than 1 in 75,000 births. Incidence is likely higher in Finland where the carrier rate is 1:175.

✓ Genetics of LCHAD Deficiency

Mutations in the HADHA gene cause long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency. Mutations in the HADHA gene lead to low levels of long-chain 3-hydroxyacyl-CoA dehydrogenase, which is part of a protein complex known as mitochondrial trifunctional protein. Long-chain fatty acids from food and body fat cannot be metabolized and processed without sufficient levels of this enzyme.

✓ Inheritance Patterns

LCHAD deficiency is inherited in an autosomal recessive pattern. Parents of a child diagnosed with LCHAD deficiency are unaffected. These individuals are carriers of the condition and have one normal HADHA gene and one abnormal HADHA gene. Each pregnancy between carrier parents has a 25% chance of producing a child affected with LCHAD deficiency, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Treatment for LCHAD deficiency involves avoiding long periods of fasting and having frequent meals that are high in carbohydrates and low in fat. Infants should have at least one nighttime feeding, or a late-night snack as they get older, to reduce the time they go without eating. Treatment should begin shortly after birth and is life-long. Some doctors may also prescribe dietary supplements. Emergency care must be taken if a person with LCHAD deficiency becomes ill and has difficulty keeping food down. This is usually treated in the hospital. People with LCHAD

deficiency require treatment through a specialty clinic with experience in treating this disorder. **Parents should always travel with a letter from the child's physician, including treatment guidelines, for any situation that may necessitate hospital admission during an acute illness.**

- ✓ **Screening Methodology**

Newborn screening for LCHAD deficiency is performed by tandem mass spectrometry (MS/MS). The primary marker for LCHAD deficiency is C16-OH**.**

- ✓ **What to do After Receiving Presumptive Positive Long chain 3-hydroxyacyl-CoA dehydrogenase Deficiency Screening Results: MEDICAL EMERGENCY - TAKE THE FOLLOWING IMMEDIATE ACTIONS:**

1) **Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, and lethargy).**
2) **Consult with pediatric metabolic specialist.**
3) **Evaluate infant (hepatomegaly, cardiac insufficiency; history of sudden unexpected death in a sibling; maternal liver disease during pregnancy; hypoglycemia). If signs are present or infant is ill, initiate emergency treatment in consultation with metabolic specialist.**
4) **Educate family about signs and symptoms of hypoglycemia and metabolic acidosis.**
5) **Report findings to Kansas Newborn Screening program.**
6) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
7) **Report Clinical Findings to Newborn Screening Program at 785-291-3363.**

- ✓ **Confirmation of Diagnosis**

Plasma acylcarnitine and urine organic acid analysis are ordered to determine if the appropriate LCAHDD/TFP profiles are present. Differentiation between both disorders requires further biochemical and molecular genetic testing in cultured fibroblasts derived from a skin biopsy. Mutation analysis of the HADHA gene is also available.

- ✓ **Communication of Results to Parents**

If a baby has a presumptive positive LCHAD deficiency newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with LCHAD deficiency, the following points should be conveyed to parents:

- ***Parents should understand that treatment is lifelong and that compliance with diet and avoidance of fasting and prolonged strenuous exercise is critical.***
- ***Although children with LCHAD deficiency are usually healthy, any illness (for example, fever, vomiting or injury) where the child is not eating requires prompt notification of the child's physician.***
- ***Parents should be encouraged to keep an individualized written treatment protocol for doctors to utilize in a medical crisis.***
- ***The siblings of a baby with LCHAD deficiency have a chance of being affected, even if they haven't had symptoms. Finding out whether other children in the family have LCHAD deficiency is important because early treatment may prevent serious health problems.***
- ***People with LCHAD deficiency typically receive follow-up care by a team of professionals that is experienced in treating people with metabolic disorders.***
- ***Parents may want to consider a medical emergency bracelet for their child.***

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