

<b>Disease Name</b>	<b>Trifunctional protein deficiency</b>
<b>Alternate name(s)</b>	N/A
<b>Acronym</b>	LCHADD/TFP
<b>Disease Classification</b>	Fatty Acid Oxidation Disorder
<b>Variants</b>	Yes
<b>Variant name</b>	Mitochondrial trifunctional protein deficiency
<b>Symptom onset</b>	Neonatal, infancy
<b>Symptoms</b>	Hypoketotic hypoglycemia, hypotonia, cardiomyopathy, hepatic disease, peripheral neuropathy and pigmentary retinopathy, rhabdomyolysis, sudden death
<b>Natural history without treatment</b>	Possible developmental delay due to damage from hypoglycemic episodes, possible death due to cardiomyopathy or hepatic failure.
<b>Natural history with treatment</b>	Intelligence is usually normal if there is no damage due to hypoglycemic crisis. Peripheral neuropathy, if present, may not improve with treatment.
<b>Treatment</b>	Avoidance of fasting, use of uncooked starch, MCT treatments, carnitine supplementation, DHA supplementation (may prevent retinopathy, but this has not been proven)
<b>Other</b>	Maternal complications in pregnancy include acute fatty liver of pregnancy, HELLP syndrome, and pre-eclampsia
<b>Physical phenotype</b>	Hypotonia, cardiomyopathy and possible retinal changes
<b>Inheritance</b>	Autosomal recessive
<b>General population incidence</b>	Rare
<b>Ethnic differences</b>	Yes
<b>Population</b>	Finnish
<b>Ethnic incidence</b>	1:240 carrier rate for common mutation G1528C in Finland
<b>Enzyme location</b>	Inner mitochondrial membrane, liver, heart, fibroblasts
<b>Enzyme Function</b>	Metabolizes long chain fatty acids (C-12 to C-16 in length)
<b>Missing Enzyme</b>	Long-chain 3-hydroxyacyl-CoA dehydrogenase or mitochondrial trifunctional protein
<b>Metabolite changes</b>	Increased 3-hydroxydicarboxylic acids in urine, increased saturated and unsaturated 3-hydroxy organic acids, possible elevated CPK during acute illness.
<b>Prenatal testing</b>	Enzyme analysis, protein analysis and direct DNA (when applicable).
<b>MS/MS Profile</b>	C18:OH, C16:1OH, C16OH
<b>OMIM Link</b>	<a href="http://www.ncbi.nlm.nih.gov/omim/600890">http://www.ncbi.nlm.nih.gov/omim/600890</a>
<b>Genetests Link</b>	<a href="http://www.genetests.org">www.genetests.org</a>
<b>Support Group</b>	FOD Family Support Group <a href="http://www.fodsupport.org">http://www.fodsupport.org</a> Save Babies through Screening Foundation <a href="http://www.savebabies.org">http://www.savebabies.org</a>  Genetic Alliance <a href="http://www.geneticalliance.org">http://www.geneticalliance.org</a>

## Newborn Screening ACT Sheet [Elevated C16-OH +/- C18 and Other Long Chain Acylcarnitines] Long-chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency (LCHADD)

**Differential Diagnosis:** Long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency; Trifunctional protein (TFP) deficiency.

**Condition Description:** LCHADD and TFP deficiencies are fatty acid oxidation (FAO) disorders. Fatty acid oxidation occurs during prolonged fasting and/or periods of increased energy demands (fever, stress) after glycogen stores become depleted and energy production relies increasingly on fat metabolism. Fatty acids and potentially toxic derivatives accumulate in FAO disorders which are caused by deficiency in one of the enzymes involved in FAO.

### **YOU SHOULD TAKE THE FOLLOWING ACTIONS:**

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy).
- Consult with pediatric metabolic specialist.
- 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.
- Educate family about need for infant to avoid fasting. Even if the infant becomes mildly ill (poor feeding, vomiting, or lethargy), immediate treatment with IV glucose is needed.
- Report findings to newborn screening program.

**Diagnostic Evaluation:** Plasma acylcarnitine analysis will show a characteristic pattern consistent with LCHADD or TFP deficiency. Urine organic acid analysis may also show an abnormal profile. Differentiation between both disorders requires further biochemical and molecular genetic testing

**Clinical Considerations:** LCHAD and TFP deficiencies may present acutely and are then associated with high mortality unless treated promptly. Hallmark features include hepatomegaly, cardiomyopathy, lethargy, hypoketotic hypoglycemia, elevated liver transaminases, elevated creatine phosphokinase (CPK), lactic acidosis, and failure to thrive. Rhabdomyolysis (a serious and sometimes fatal complication) may occur. Milder variants exist. Consider that cefotaxime treatment in the baby or mother may alter lab results.

### **Additional Information:**

[Emergency Treatment Protocol \(New England Consortium of Metabolic Programs\)](#)

Genetics Home Reference:

[LCHAD](#)

[TFP](#)

### **Referral (local, state, regional and national):**

[Testing](#)

[Clinical Services](#)

Disclaimer: This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. Adherence to this guideline does not necessarily ensure a successful medical outcome. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.

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