

<b>Disease Name</b>	
<b>LONG-CHAIN HYDROXYACYL-CoA DEHYDROGENASE (LCHAD)</b>	
(LCHAD; MITOCHONDRIAL TRIFUNCTIONAL PROTEIN DEFECT; LONG-CHAIN HYDROXYACYL-CoA DEHYDROGENASE; LONG-CHAIN 3-HYDROXYACYL-CoA DEHYDROGENASE DEFICIENCY)	
<b>Classification:</b>	Fatty acid oxidation defect
<b>Genetic Information</b>	
<b>Inheritance:</b>	Autosomal recessive.
<b>Population Incidence:</b>	Unknown.
<b>Ethnic Incidence:</b>	Increased in Finland with the carrier frequency of the most common allele at 1:175.
<b>Gene &amp; Location:</b>	HADHA, MTPA, HADHB genes involved on 2q23
<b>Common Mutation:</b>	1528G>C- (E510Q) E474 common in isolated LCHAD.
<b>OMIM #</b>	*600890 LCHAD; *143450 TFP
<b>Disease Information</b>	
<b>Symptom Onset:</b>	Age of onset ranges from neonate to several years of age with a mean age at presentation of 5.8 months. Fifteen percent present in the neonatal period.
<b>Symptoms:</b>	<p>There are three phenotypes: <b>severe neonatal form</b>, universally fatal with cardiac involvement; <b>infancy onset hepatic</b> presentation and milder, later-onset with neuromyopathic phenotype. Close review of symptoms will reveal chronic, non-specific symptoms like hypotonia, failure to thrive and feeding problems preceded the hypoglycemia and acute presentation in the majority of patients. Death from heart, respiratory or liver failure can occur despite aggressive support. In survivors, psychomotor development is generally normal, but damage can occur from unrecognized hypoglycemia. Episodes of myoglobinuria with exercise, progressive peripheral neuropathy and progressive retinal pigmentation with vision loss occur in childhood. A significant number of patients have had anemia or thrombocytopenia. Hypoparathyroidism is another complication.</p> <p>Maternal pregnancy complications include HELLP or acute fatty liver of pregnancy (AFLP) in 20 percent of affected LCHAD fetuses.</p>
<b>Physical Findings:</b>	Cardiomyopathy and retinal changes; no other dysmorphic features.
<b>Treatment:</b>	Frequent feedings, a diet consisting of long-chain fatty acid restriction, high carbohydrate content, MCT oil, carnitine, essential fatty acid and multivitamin supplementation have been the primary therapy. There is some evidence that use of DHA (docosahexanoic acid) can help prevent retinal degeneration.
<b>Natural History without treatment:</b>	About 50 percent of patients have died, either from the first presentation or with progressive disease. No good correlation between enzyme activity and phenotype/clinical severity. Can have either a relapsing/remitting course or chronic progression.
<b>Natural History with treatment:</b>	Despite aggressive dietary treatment and avoidance of fasting approximately 30 percent continue to have episodic decompensations. Few patients have been diagnosed early and treated prospectively.
<b>Metabolic Information</b>	
<b>Missing</b>	Missing enzyme can either be isolated long-chain 3-hydroxyacyl-CoA dehydrogenase or

<b>Enzyme &amp; Location:</b>	can be the trifunctional protein with defects in long-chain 3-hydroxyacyl-CoA dehydrogenase, long-chain 3-ketoacyl-CoA thiolase and long-chain 2-enoyl-CoA hydratase. These enzymes metabolize 3-hydroxy acyl CoA compounds with chains of 12 to 18 carbons catalyzing the last three steps in betaoxidation of long-chain fatty acids. They are bound to the inner mitochondrial membrane.	
<b>MS/MS profile:</b>	C16-OH (3-hydroxypalmitoyl carnitine)- elevated. C14:1-OH; C16; C18:1-OH or C18:1- can also be elevated.	
<b>Prenatal testing:</b>	Prenatal diagnosis is possible either with biochemical studies or with DNA testing if the mutations in the family are known.	
<b>Miscellaneous Information:</b>	Affected patients need at minimum, yearly evaluations by an ophthalmologist with retinal exams. May be a predisposition to ARDS during acute illness- a case series of four patients with LCHAD developed ARDS during the course of hospitalization.	
<b>Credit:</b>	<i>Prepared by the North West Regional Newborn Screening Program Judith Tuerck, RN, MS, and Lorinda Paradise at Oregon Health Services University in Portland, Oregon and by Sara Copeland MD, Iowa Neonatal Metabolic Screening Program.</i>	
<b>Sites of Reference:</b>	<p><b>National Library of Medicine Genetics Home Reference</b>  <u>Mitochondrial trifunctional protein deficiency</u>  <a href="http://ghr.nlm.nih.gov/condition=mitochondrialtrifunctionalproteindeficiency">http://ghr.nlm.nih.gov/condition=mitochondrialtrifunctionalproteindeficiency</a></p> <p><b>National Library of Medicine Genetics Home Reference</b>  <u>Long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency</u>  <a href="http://ghr.nlm.nih.gov/condition=longchain3hydroxyacylcoenzymeadehydrogenasedeficiency">http://ghr.nlm.nih.gov/condition=longchain3hydroxyacylcoenzymeadehydrogenasedeficiency</a></p>	
<b>Support Groups:</b>	<p><b>Save Babies Through Screening Foundation, Inc</b>  4 Manor View Circle  Malvern, PA 19355-1622  888-454-3383  610-993-0545  email@savebabies.org  <a href="http://www.savebabies.org">Trifunctional Protein Deficiency</a></p> <p><b>FOD (Fatty Oxidation Disorder) Family Support Group</b>  1559 New Garden Rd, 2E  Greensboro, NC 27410  336-547-8682  336-292-0536  deb@fodsupport.org  <a href="http://www.fodsupport.org">www.fodsupport.org</a></p>	<p><b>Children Living with Inherited Metabolic Diseases (CLIMB)</b>  Climb Building  176 Nantwich Road  Crewe, CW2 6BG  United Kingdom  (+44) 0870 7700 326  (+44) 0870 7700 327  steve@climb.org.uk  <a href="http://www.climb.org.uk">www.climb.org.uk</a></p>