

<b>Disease Name</b>	
<b>HOLOCARBOXYLASE DEFICIENCY (MCCD)</b>	
<i>(HOLOCARBOXYLASE SYNTHETASE DEFICIENCY; MULTIPLE CARBOXYLASE DEFICIENCY, NEONATAL FORM)</i>	
<b>Classification:</b>	Organic aciduria
<b>Genetic Information</b>	
<b>Inheritance:</b>	Autosomal recessive.
<b>Population Incidence:</b>	1 in 87,000 live births.
<b>Ethnic Incidence:</b>	No known population at increased risk.
<b>Gene &amp; Location:</b>	21q22.1- HLCS gene
<b>Common Mutation:</b>	Some with increased frequency in different populations.
<b>OMIM #</b>	*253270
<b>Disease Information</b>	
<b>Symptom Onset:</b>	Anytime from birth to 15 months of age.
<b>Symptoms:</b>	Infants generally present with food refusal, vomiting, breathing problems, hypotonia, seizures and lethargy. Severe metabolic/lactic acidosis, organic aciduria, mild hyperammonemia and variable hypoglycemia can lead to coma and death if not treated. Survivors can have neurological damage. Patients may have skin rash and alopecia at later stages.
<b>Physical Findings:</b>	The skin rash and alopecia. Otherwise, no particular dysmorphisms.
<b>Treatment:</b>	Majority of cases respond readily to biotin supplementation. Biotin increases the functional activation of the carboxylase enzymes.
<b>Natural History without treatment:</b>	Repeated bouts of acidosis, skin rashes, failure to thrive, coma, developmental delay and death.
<b>Natural History with treatment:</b>	Children with holocarboxylase synthetase deficiency, treated with biotin, have normal growth and development. However, some only partly respond to therapy and one has been reported to be unresponsive to biotin therapy.
<b>Metabolic Information</b>	
<b>Missing Enzyme &amp; Location:</b>	Holocarboxylase synthetase (HS) attaches biotin to the four carboxylase enzymes (pyruvate carboxylase; propionyl CoA carboxylase; beta-methylcrotonyl CoA carboxylase; acetyl CoA carboxylase) in order to activate them. Deficiency of HS results in functional deficiencies of all the carboxylase enzymes.
<b>MS/MS profile:</b>	C3 (propionyl carnitine)- elevated. C5-OH (3-hydroxyisovaleryl carnitine)- elevated.
<b>Prenatal testing:</b>	Enzyme assay of the carboxylase enzymes on amniocytes.
<b>Miscellaneous Information:</b>	
<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>	<b>OMIM - Multiple CoA Carboxylase Deficiency</b> <a href="http://www.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?253270">www.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?253270</a>  National Library of Medicine Genetics Home Reference

	<b><u>Holocarboxylase synthetase deficiency</u></b> <b><a href="http://ghr.nlm.nih.gov/condition=holocarboxylasesynthetasedeficiency">http://ghr.nlm.nih.gov/condition=holocarboxylasesynthetasedeficiency</a></b>
<b>Support Groups:</b>	<b>Organic Acidemia Association</b> www.oaaneews.org/ 13210 35th Avenue Plymouth, MN 55441 Contact: Kathy Stagni (763) 559-1797 OAANews@aol.com