

Disease Name	
CITRULLINEMIA, TYPE II	
(CITRULLINEMIA, TYPE II, ADULT-ONSET; CTLN2; CITRULLINEMIA, TYPE II, NEONATAL-ONSET; CHOLESTASIS, NEONATAL INTRAHEPATIC, CAUSED BY CITRIN DEFICIENCY)	
Classification:	Urea cycle defect
Genetic Information	
Inheritance:	Autosomal recessive.
Population Incidence:	Unknown.
Ethnic Incidence:	Of the 150 identified cases, all but seven have been in Japan.
Gene & Location:	SLC25A13 gene- 7q21.3
Common Mutation:	IVS11+1G>A- accounts for 40 percent of mutated alleles found in Japan. Second most common is 851del4. Together they account for 70 percent of patients in Japan.
OMIM #	#603471; #605814
Disease Information	
Symptom Onset:	The neonatal intrahepatic cholestasis develops between one to five months of age. The adult onset 11-64 years of age.
Symptoms:	<p>Neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD) has been diagnosed in over 70 infants between one to five months of age. In addition to intrahepatic cholestasis, they have jaundice and fatty liver at biopsy. Liver disease generally resolves by one year of age. Three patients developed liver failure necessitating transplants before 12 months of age.</p> <p>Among patients with CTLN2 presentation may be in childhood or adulthood (11-64 years). Symptoms may be acute or develop gradually and include enuresis, delayed menarche, insomnia, nocturnal sweats and terrors, recurrent vomiting, diarrhea, tremors, confusion, lethargy, convulsions, delusions, hallucinations and episodes of coma. Hypercitrullinemia and hyperammonemia are present. Pancreatitis, hyperlipidemia or death from cerebral edema generally occurs within a few years of the diagnosis. Hepatocellular carcinoma has been reported in a few cases.</p>
Physical Findings:	No dysmorphisms. Only physical findings are related to the cholestasis or the psychological findings in adulthood.
Treatment:	Treatment of choice is liver transplant in the adult form, it is not known if the neonatal form patients will go on to develop the adult form. Neonatal symptoms tend to resolve with protein restriction. Arginine may help ameliorate the symptoms.
Natural History without treatment:	The neonatal form may resolve. The adult form progresses to death.
Natural History with treatment:	Liver transplantation may cure the disorder.
Metabolic Information	
Missing Enzyme & Location:	Citrin is a calcium dependent mitochondrial aspartate glutamate transporter that inactivates argininosuccinate synthetase activity only in the liver, presumably by disrupting mitochondrial export of aspartate and from defects in the malate aspartate shuttle.
MS/MS profile:	Citrulline- elevated.

Prenatal testing:	Possible to do enzyme assay in at risk pregnancy with amniocytes or CVS.	
Miscellaneous Information:		
Credit:	<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>	
Sites of Reference:	<p>Citrullinemia - Ped Base www.icndata.com/health/pedbase/files/CITRULLI.HTM</p> <p>NORD - Citrullinemia www.rarediseases.org/search/rdbdetail_abstract.html?disname=Citrullinemia</p> <p>OMIM - CITRULLINEMIA www3.ncbi.nlm.nih.gov/htbin-post/Omim/dispim?215700</p> <p>TRUE Kids (Transplanted to Resolve a Urea-cycle Enzyme-deficiency) www.truekids.org/</p>	
Support Groups:	<p>National Urea Cycle Disorders Foundation 4841 Hill Street La Canada, CA 91011 www.nucdf.org/ 1-800-38NUCDF Contact: Cynthia LeMons cindy@nucdf.org</p>	