

Disease Name	
GLUTARIC ACIDURIA TYPE I (GA I)	
<i>(GA I; GLUTARIC ACIDURIA I; GLUTARYL-CoA DEHYDROGENASE DEFICIENCY)</i>	
Classification:	Organic aciduria
Genetic Information	
Inheritance:	Autosomal recessive
Population Incidence:	1:40,000 in Caucasians; 1:30,000 in Sweden; 1:300 in Old Order Amish.
Ethnic Incidence:	1/10 carrier frequency among certain inbred populations, particularly the Old Order Amish in Pennsylvania and the Ojibway Indians in Canada.
Gene & Location:	GCDH; 19p13.2
Common Mutation:	No common mutation, with the exception of the above mentioned populations.
OMIM #	*231670
Disease Information	
Symptom Onset:	Infancy, typically 2-37 months.
Symptoms:	Seventy percent of patients have macrocephaly at or shortly after birth. There may be soft neurologic signs like jitteriness, irritability, and truncal hypotonia in the newborn period. There are several different clinical presentations: 1) Affected infants appear normal and then suffer an acute metabolic crisis, usually 6-18 months (90 percent of acute crises in first 24 months of life), with subsequent neurological findings that improve slightly then remain static. Changes in the basal ganglia in particular, atrophy of the caudate and putamen develop within a few days or weeks of encephalopathic episode; 2) Infants have a period of normal development, acute crisis and subsequent neurological findings similar to those above, but then progress slowly with recurrent episodes of ketosis, vomiting, hepatomegaly and encephalopathy when the child develops infections; 3) Approximately 25 percent of infants gradually develop motor delay, hypotonia, dystonia and dyskinesia during the first few years of life without any apparent acute crisis; and 4) Individuals can be completely asymptomatic without any crises and normal development. This has been documented via carrier testing and identification of five percent of affected Amish without symptoms. Some of these adults have now been diagnosed with white matter changes.
Physical Findings:	Macrocephaly, cerebral palsy, dystonia.
Treatment:	Prompt treatment of catabolic events with fever control, IVF, glucose, insulin and carnitine may prevent neurologic symptoms in patients without striatal damage at diagnosis. The effect of treatment with riboflavin and diet restriction of lysine and tryptophan is less clear. Hospital admission is mandatory for IV fluids with any vomiting or febrile illness. Patients appear to do better if started on high-dose IV carnitine during illnesses.
Natural History without treatment:	Presymptomatic diagnosis has proven to have a better outcome than identifying patients after their first encephalopathic event.
Natural History with treatment:	Even with prospective treatment up to thirty five percent of patients will have neurological insult and disability.
Metabolic Information	
Missing Enzyme & Location:	Glutaryl-coenzyme A dehydrogenase found in the mitochondria; liver, kidney and fibroblasts and leukocytes- catalyzes the oxidative decarboxylation of glutaryl-CoA to crotonyl-CoA.
MS/MS profile:	C5-DC (glutaryl carnitine)- elevated- can be missed in some patients.
Prenatal testing:	Yes. Enzyme activity in CVS and amniocytes.
Miscellaneous	Neuroradiographic findings of frontal-temporal atrophy and/or arachnoid cysts before the onset of

Information:	<p>symptoms. Infants with GA I are prone to suffer acute subdural hemorrhages and retinal hemorrhages after minor head trauma, i.e. commonly around the first birthday when starting to walk. This can be misdiagnosed as child abuse. In this population, 20-30 percent of patients have “chronic” subdural effusions and hematomas identified on neuroimaging studies; these are always found in the presence of atrophy and extra cerebral fluid. At least two patients with GA I have developed rhabdomyolysis after fairly mild infections.</p> <p>Currently there is a prospective study to treat and follow these children www.stoffwechsel.uni-hd.de/unis/start_1.htm</p>	
Credit:	<p><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></p>	
Sites of Reference:	<p>Allison's GA-I Website - A Personal Story www.ga1.freesevers.com/</p> <p>Dietary Specialist - Low Protein Foods www.dietspec.com/</p> <p>MUMS - National Parent-to-Parent Network www.netnet.net/mums/</p> <p>National Organization of Rare Disorders - glutaric aciduria 1 www.rarediseases.org/search/rdbdetail_abstract.html?disname=Glutaricaciduria%20I</p> <p>OMIM - Glutaric Acidemia Type I www3.ncbi.nlm.nih.gov/htbin-post/Omim/dispnim?231670</p> <p>Organization For Endocrine & Metabolic Diseases www.niddk.nih.gov/health/endo/pubs/endorg/endorg.htm</p> <p>Pediatric Database - Glutaric Aciduria www.icondata.com/health/pedbase/files/glutaric.htm</p>	
Support Groups:	<p>International Organization for Glutaric Acidemia (IOGA) Contact: Cay Welch www.glutaricacidemia.org cswelch@helicon.net (724) 459-0179</p> <p>Organic Acidemia Association 13210 35th Avenue Plymouth, MN 55441 Contact: Kathy Stagni (763) 559-1797 OAANews@aol.com www.oaanews.org</p>	<p>International Organization for Glutaric Acidemia RD #4, Box 299-A Blairsville, PA 15717 Contact: Michael Metil (724) 459-0179 mmetil@helicon.net</p>