

| | |
|--|--|
| Disease Name | Glutaric acidemia type 2 |
| Alternate name(s) | Glutaric aciduria II, Glutaryl-CoA dehydrogenase deficiency |
| Acronym | GA2, GA-II |
| Disease Classification | Organic Acid Disorder |
| Variants | Yes |
| Variant name | Riboflavin responsive GA1 |
| Symptom onset | Infancy (typically 2- 37 months) |
| Symptoms | Macrocephaly may be present at birth, acute encephalitic-like crises; neurodegenerative disorder with spasticity, dystonia, choreoathetosis, ataxia and dyskinesia, seizures, hypotonia, death due to Reye-like syndrome. |
| Natural history without treatment | Possible developmental delay due to encephalitis-like crisis; neurologic deterioration including spasticity, dystonic cerebral palsy. May have neurologic signs with normal IQ. Some individuals may be asymptomatic. |
| Natural history with treatment | If instituted before any damage occurs, normal outcome may occur. Risk for neurologic damage is highest in first few years. Some evidence that treatment may slow neurologic deterioration. |
| Treatment | Lysine and tryptophan restricted diet, riboflavin supplementation, carnitine supplementation. Rapid treatment of intercurrent illness with intravenous glucose, carnitine and appropriate supportive measures. |
| Other | Profuse sweating has been reported. Neuroradiographic findings of frontotemporal atrophy on CT or MRI with increased CSF containing spaces in the sylvian fissures and anterior to the temporal lobes. Also decreased attenuation in cerebral white matter on CT and increased signal intensity on MRI. Basal ganglia changes. |
| Physical phenotype | Macrocephaly, cerebral palsy |
| Inheritance | Autosomal recessive |
| General population incidence | 1:40,000 in Caucasians and 1:30,000 in Sweden |
| Ethnic differences | Yes |
| Population | Old Amish and Ojibway Indians in Canada |
| Ethnic incidence | 1/10 carrier frequency |
| Enzyme location | Mitochondria; liver, kidney, fibroblasts and leukocytes |
| Enzyme Function | Metabolizes lysine, hydroxylysine and tryptophan |
| Missing Enzyme | Glutaryl-CoA dehydrogenase |
| Metabolite changes | Increased glutaric acid in urine, increased glutaric acid and 3-hydroxyglutaric acid in plasma, 3-hydroxyglutaric and glutaconic acid in urine. |
| Prenatal testing | Enzyme activity in CVS and amniocytes |
| MS/MS Profile | Elevated C5DC - can be missed some patients |
| OMIM Link | http://www.ncbi.nlm.nih.gov/omim/231670 |
| Genetests Link | www.genetests.org |
| Support Group | Organic Acidemia Association www.oaanews.org Save Babies through Screening Foundation www.savebabies.org Genetic Alliance www.geneticalliance.org |

Newborn Screening ACT Sheet [Elevated C5-DC Acylcarnitine] Glutaryl-CoA Dehydrogenase Deficiency

Differential Diagnosis: Glutaric aciduria (GA-1)

Condition Description: GA-1 is caused by a defect of glutaryl-CoA dehydrogenase which limits the metabolism of glutaryl-CoA to crotonyl-CoA, resulting in increased glutaric acid or its metabolites that are toxic.

YOU SHOULD TAKE THE FOLLOWING ACTIONS:

- Contact family IMMEDIATELY to inform them of the newborn screening result.
- Consult with pediatric metabolic specialist.
- Evaluate the newborn for macrocephaly and muscle hypotonia, initiate confirmatory/diagnostic testing as recommended by metabolic specialist.
- Refer to metabolic specialist to be seen as soon as possible but not later than three weeks.
- Educate family about diagnostic possibilities, complexity of diagnostic work-up and the possibility of neurodegenerative crisis with an intercurrent infectious illness.
- IMMEDIATE treatment with IV glucose is needed for intercurrent infectious illness.
- Report findings to newborn screening program.

Diagnostic Evaluation: Urine organic acid analysis should be ordered promptly, and will be diagnostic if it shows increased 3-hydroxyglutaric acid with or without increased glutaric acid. If urine organic acids don't confirm the diagnosis, the metabolic specialist will consider analyzing glutarylcarnitine in urine and 3-hydroxyglutaric acid in blood and CSF, enzyme assay in fibroblasts, and molecular analysis of the GCDH gene.

Clinical Considerations: The neonate with glutaric acidemia type I is usually macrocephalic but otherwise asymptomatic. Later signs include metabolic ketoacidosis, failure to thrive, and sudden onset of dystonia and athetosis due to irreversible striatal damage. With appropriate treatment, 60-70% of patients will not suffer neurodegenerative disease.

Additional Information:

[Gene Reviews](#)
[Genetics Home Reference](#)

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.

© American College of Medical Genetics, 2010 (Funded in part through MCHB/HRSA/HHS grant #U22MC03957)

