



## **Glutaric Aciduria, Type 1 Information for Health Professionals**

Glutaric aciduria, type 1 is an organic acid disorder where individuals cannot metabolize the amino acids lysine, hydroxylysine and tryptophan. Deficiency of the enzyme Glutaryl-CoA dehydrogenase causes this form of glutaric aciduria.

### ✓ **Clinical Symptoms**

Symptoms generally begin between two months and four years of age, though some infants may be born with macrocephaly. Isolated macrocephaly can be a benign familial trait. Glutaric aciduria, type 1 causes periods of metabolic crisis. Early symptoms of a crisis include feeding difficulties, irritability, vomiting, lethargy, and hypertonia. If untreated, symptoms include muscle spasms, spasticity, metabolic acidosis, dystonia, seizures, subdural hematomas, coma, and death. Metabolic crises can be triggered by illness/infection, fever, or fasting. Crises are less common as the child ages.

Even without a metabolic crisis, symptoms may include: failure to thrive, hepatomegaly, hypotonia, progressive spasticity, dystonia, fevers, developmental delay, learning delays or intellectual disabilities, and speech problems.

### ✓ **Incidence**

Glutaric aciduria, type 1 occurs in greater than 1 in 75,000 Caucasian live births. There is an increased incidence in the Amish, the Ojibway population of Canada, and people with Swedish ancestry.

### ✓ **Genetics of glutaric aciduria type 1**

Mutations in the GCDH gene cause glutaric aciduria, type 1. Mutations in this gene reduce or eliminate the activity of glutaryl-CoA dehydrogenase. This enzyme is necessary in breaking down glutaryl-CoA, which is produced during the metabolism of the amino acids lysine, tryptophan, and hydroxylysine. This causes the accumulation of glutaric acid in the blood and results in the symptoms of this condition. This accumulation is especially damaging to the basal ganglia, which causes the movement symptoms seen in this condition.

### ✓ **How do people inherit glutaric aciduria, type 1?**

Glutaric aciduria, type 1 is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with glutaric aciduria, type 1, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

### ✓ **Treatment**

Immediate diagnosis and treatment of glutaric aciduria, type 1 is critical for normal growth and development. Affected individuals should follow a diet that is low in lysine and tryptophan, which generally requires medical foods and formulas. L-carnitine and riboflavin supplementation may be recommended. Symptoms of a metabolic crisis require immediate medical treatment, which may require IV medications such as glucose, carnitine, and others. Individuals should avoid fasting and have regular blood and urine tests to measure amino acid levels.

✓ **Screening Methodology**

Primary newborn screening for glutaric aciduria, type 1 utilizes tandem mass spectrometry. Elevated C5-DC (glutaryl carnitine) indicates the possibility of glutaric aciduria, type 1. False positive and false negative results are possible with this screen.

✓ **What to do After Receiving Presumptive Positive GA-1 Screening Results**

- 1) The clinician should immediately check on the clinical status of the baby.
- 2) Consultation with a metabolic specialist is essential.
- 3) The specialist may request urine organic acid analysis and other labs on the baby.
- 4) Call the KS Newborn Screening Program at 785-291-3363 with questions about results.
- 5) Report clinical findings to the Newborn Screening Program at 785-291-3363.
- 6) Same birth siblings (twins, triplets) of infants diagnosed with glutaric aciduria, type 1 should be re-screened; additional testing of these siblings also may be indicated.
- 7) Consider testing older siblings. Some individuals may show no symptoms and will go undiagnosed.

✓ **Confirmation of Diagnosis**

The diagnosis of glutaric aciduria, type 1 is confirmed through urine organic acid analysis revealing elevated glutaric acid and 3-hydroxyglutaric acid. If this is not confirmatory, 3-hydroxyglutaric acid in blood and CSF, urine glutarylcarnitine, enzyme analysis using fibroblasts, or molecular analysis can diagnose this condition.

✓ **Communication of Results to Parents**

**If a baby has a presumptive positive glutaric aciduria, type 1 newborn screening result, additional testing needs to be performed to confirm a diagnosis.** In accordance with the Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with glutaric aciduria, type 1 the following points should be conveyed to parents:

- ***Parents should understand that treatment for glutaric aciduria type 1 will be lifelong.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include pediatric, metabolic specialists, and dieticians.***
- ***Genetics counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation contact:

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