



**State of CT  
Genetics Newborn Screening Program  
Health Care Provider Fact Sheet**

**Glutaric Acidemia Type I (GA I)**

Glutaric acidemia, type I (GA-I) is an autosomal recessive inborn error of metabolism and is caused by the deficiency of glutaryl-CoA dehydrogenase, an essential enzyme in the catabolism of the amino acids tryptophan, lysine, and hydroxylysine. This enzyme deficiency disorder is characterized by hypoglycemia, dystonia, and dyskinesia. After a period of apparently normal development, the disorder may appear suddenly and present as a toxic encephalopathy. Symptoms include vomiting, poor feeding, neurologic symptoms such as seizures and abnormal tone, and lethargy progressing to coma. Additional neurologic findings may include repetitive movements or abnormal posturing. Despite slow improvement, many patients do not fully recover from a neurologic crisis.

The most significant physical sign in GA-I is macrocephaly; in fact, macrocephaly may be the only physical sign in otherwise asymptomatic infants. 70% of patients have macrocephaly at or shortly after birth. Most commonly, infants develop progressive macrocephaly with markedly accelerated rates of head circumference growth in the first few months of life.

There are several different clinical presentations: 1). Affected infants appear normal and then suffer an acute metabolic crisis, usually 6-18 months, with subsequent neurological findings that improve slightly then remain static. Changes in the basal ganglia in particular, atrophy of the caudate and putamen develops within a few days or weeks of encephalopathic episode. Neuronal loss and fibrous gliosis occur in the caudate and putamen as part of neurotoxicity of GA I. 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% of infants gradually develop motor delay, hypotonia, dystonia and dyskinesia during the first few years of life without any apparent acute crisis. 4). Individuals can be completely asymptomatic without any crises and normal development.

Neuroradiographic findings of frontal-temporal atrophy and/or arachnoid cysts before the onset of symptoms may be seen. 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% 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.

**Diagnosis**

Newborn screening—Tandem mass spectrometry: C5DC

Confirmation—a second sample may be requested or follow up testing will be done at the Metabolic Treatment Center at Yale or UCONN Genetics.

**Situations that risk metabolic decompensation**

Fasting, intercurrent illness, post vaccination, surgery

## Monitoring

Clinical observation is the most important tool for monitoring patients with GA I. It is important for the primary care provider and the Metabolic Treatment Center to develop an on-going collaborative relationship in caring for these patients.

## Treatment

- Restricting dietary lysine and tryptophan rather than restricting total protein allows a greater intake of overall nitrogen
- Pharmacologic doses of riboflavin which serves as a cofactor for glutaryl-CoA dehydrogenase and facilitates any residual enzyme activity
- Carnitine supplementation has been shown to increase the urinary excretion of glutaric acid and replenish reduced body carnitine stores
- During an acute neurologic crisis, additional protein restriction and carbohydrate supplementation are introduced to prevent or reverse endogenous protein catabolism.
- The parents usually have an emergency protocol with them. This protocol, provided by the Metabolic Treatment Center, contains basic information about the disorder, necessary diagnostic investigations and guidelines for treatment.
- Infants and children with GA I should have regularly scheduled visits at the Metabolic Treatment Center.

## Illness And Immunization

Intercurrent illnesses and vaccinations may aggravate hypotonia, unusual hand movements and posturing but are usually reversible and of little clinical significance though may precipitate crises (usually after first birthday). Prevention and/or early intervention is of particular importance. For this and other reasons **immunizations must be kept on track**. There is no contraindication to immunization because of GA I, but patients and physicians should be alerted to the need for immediate evaluation if high fever, lethargy or vomiting occurs in the first 24h. The Metabolic Treatment Center should be consulted with within 24 hours of the onset of the illness.

## Surgical/surgical procedures

Pre-operative fasting can precipitate encephalopathic crises

## Growth and development

Intellectually intact, however, capabilities are dependant on avoidance of metabolic decompensation.



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