



Organic Acid Disorders

Screening, Technology, and Research in Genetics is a multi-state project to improve information about the financial, ethical, legal, and social issues surrounding expanded newborn screening and genetic testing – <http://www.newbornscreening.info>

Disease name: Glutaric acidemia, type 1

Acronym: GA-1

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This fact sheet contains general information about GA-1. Every child is different and some of these facts may not apply to your child specifically. Certain treatments may be recommended for some children but not others. All children with GA-1 should be followed by a metabolic doctor in addition to their primary doctor.

What is GA-1?

GA-1 stands for “glutaric acidemia, type 1”. It is one type of organic acid disorder. People with GA-1 have problems breaking down the amino acids lysine, and tryptophan from the food they eat.

Organic Acid Disorders:

Organic acid disorders (OAs) are a group of rare inherited conditions. They are caused by enzymes that do not work properly. A number of enzymes are needed to process protein from the food we eat for use by the body. Problems with one or more of these enzymes can cause an organic acid disorder.

People with organic acid disorders cannot break down protein properly. This causes harmful substances to build up in their blood and urine. These substances can affect health, growth and learning.

The symptoms and treatment vary between different organic acid disorders. They can also vary from person to person with the same organic acid disorder. See the fact sheets for each specific organic acid disorder.

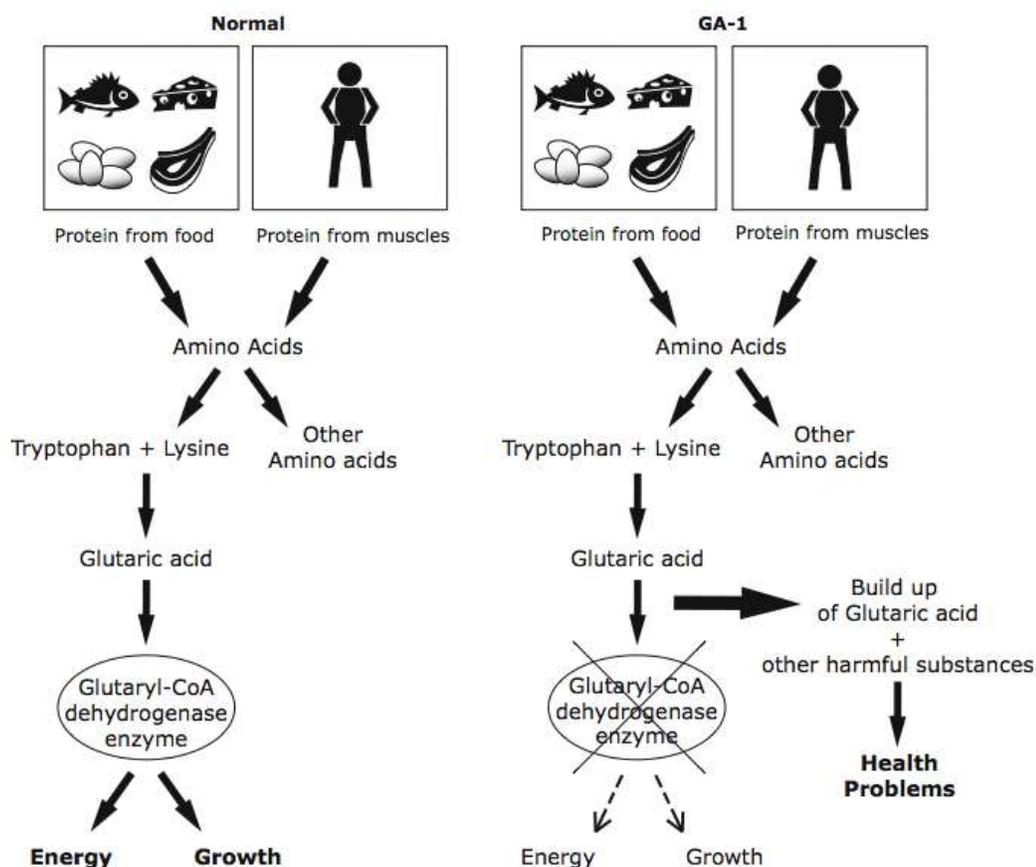
Organic acid disorders are inherited in an autosomal recessive manner and affect both males and females.

What causes GA-1?

In order for the body to use protein from the food we eat, it is broken down into smaller parts called amino acids. Special enzymes then make changes to the amino acids so the body can use them.

GA-1 occurs when an enzyme called "glutaryl-CoA dehydrogenase" is either missing or not working properly. This enzyme's job is to break down a substance called glutaryl-CoA. Glutaryl-CoA is made when the amino acids lysine, hydroxylysine and tryptophan are processed. It cannot be removed and it causes glutaric acid and other harmful substances build up in the blood and cause problems. Lysine and tryptophan are found in all foods that contain protein.

Glutaric Acidemia - type 1 (GA-1)



If GA-1 is not treated, what problems occur?

Babies with GA-1 are usually healthy at birth, although many are born with a larger than average head size. Other symptoms usually start between two months and four years of age.

GA-1 causes episodes of severe illness called metabolic crises. Some of the first symptoms of a metabolic crisis are:

- poor appetite
- extreme sleepiness or lack of energy
- irritability
- jitteriness
- nausea
- vomiting
- low muscle tone (floppy muscles and joints)
- muscle weakness

If untreated, other symptoms then follow:

- tics or spasms of the muscles
- rigid muscle contractions called spasticity
- involuntary jerking movements of the arms and legs, called dystonia
- poor coordination and balance problems
- increased levels of acidic substances in the blood, called metabolic acidosis
- seizures
- swelling of the brain or blood in the brain
- coma, sometimes leading to death

Episodes of metabolic crisis are often triggered by:

- illness or infection
- fever
- going without food for long periods of time

Other effects of GA-1 that can happen even without a metabolic crisis are:

- poor growth
- enlarged liver
- low muscle tone
- progressive spasticity
- dystonia, an involuntary movement disorder
- repeated episodes of fever
- excessive sweating
- delays in walking and other motor skills
- learning delays and intellectual disabilities
- speech problems
- brain damage

Some people have very mild or no symptoms and are only found to be affected after a brother or sister is diagnosed.

What is the treatment for GA-1?

Your baby's primary doctor will work with a metabolic doctor and a dietician to care for your child.

Prompt treatment is needed to prevent episodes of metabolic crisis. You need to start treatment as soon as you know your child has GA-1. Certain treatments may be advised for some children but not others. Treatment is usually needed throughout life.

The following are treatments often recommended for babies and children with GA-1:

1. Medication

Riboflavin is a vitamin that helps the body process protein. It may also help lessen the amount of glutaric acid made by the body. Your doctor may recommend that your child take riboflavin supplements by mouth.

Some children may be helped by L-carnitine. This is a safe and natural substance that helps body cells make energy. It also helps the body get rid of harmful wastes. Your doctor will decide whether or not your child needs L-carnitine supplements. Unless you are advised otherwise, use only L-carnitine prescribed by your doctor.

Do not use any medication without checking with your metabolic doctor.

Children with symptoms of a metabolic crisis need medical treatment right away. They often need to be treated in the hospital. During a metabolic crisis, children may be given fluids, glucose, insulin, carnitine and other medications by IV to help get rid of harmful substances in the blood. Ask your metabolic doctor if you should carry a special travel letter with medical instructions for your child's care.

2. Avoid going a long time without food

Infants and young children with GA-1 need to eat frequently to prevent a metabolic crisis. Your metabolic doctor will tell you how often your child needs to be fed. In general, it is often suggested that infants be fed every four to six hours. Some babies need to eat even more frequently than this. It is important that infants be fed during the night. They may need to be woken up to eat if they do not wake up on their own. Your metabolic doctor and dietician will give you an appropriate feeding plan for your infant. Your doctor will also give you a 'sick day' plan, tailored to your child's needs, for you to follow during illnesses or other times when your child will not eat.

Your metabolic doctor will continue to advise you on how often your child should eat as he or she gets older. When they are well, many older children and adults with GA-1 can go without food for up to 12 hours without problems. They may need to continue the other treatments throughout life.

3. Food plan, including medical foods and formula

Most children need to eat a diet made up of foods low in lysine and tryptophan. Special medical foods and a special formula are usually part of the diet. Your dietician will create a food plan that has the right amount of protein, nutrients, and energy for your child.

Low-protein (lysine and tryptophan) diet

Foods that will need to be avoided or strictly limited include:

- milk, cheese, and other dairy products
- meat and poultry

- fish
- eggs
- dried beans and legumes
- nuts and peanut butter

Many vegetables and fruits have only small amounts of lysine and tryptophan and can be eaten in carefully measured amounts.

Do not remove all protein from the diet. Your child still needs a certain amount of protein for normal growth and development. Any changes in the diet should be made under the guidance of a dietician familiar with GA-1.

Medical foods and formula

There are medical foods such as special low-protein flours, pastas, and rice that are made especially for people with organic acid disorders.

A special medical formula that contains the right level of amino acids and nutrients for your child may be recommended. Your metabolic doctor and dietician will tell you whether your child should be on this formula and how much to use. Some states offer help with payment, or require private insurance to pay for the formula and other special medical foods.

Your child's exact food plan will depend on many things such as his or her age, weight, general health, and blood test results. Your dietician will fine-tune your child's diet over time.

The long-term benefits of the special diet and medical foods are not yet known. However, it is important to follow the food plan as long as your doctor advises.

4. Regular blood tests

Your child will have regular blood tests to measure his or her amino acid levels. Urine tests may also be done. Your child's diet and medication may need to be adjusted based on blood and urine test results.

5. Call your doctor at the start of any illness

For some babies and children, even minor illness can lead to a metabolic crisis. In order to prevent problems, call your doctor right away when your child has any of the following:

- loss of appetite
- low energy or extreme sleepiness
- vomiting
- fever
- infection or illness
- behavior or personality changes

Children with GA-1 need to eat more carbohydrates and drink more fluids when they are ill – even if they're not hungry – or they could have a metabolic crisis.

Children who are sick often don't want to eat. If they can't eat, or if they show signs of a metabolic crisis, they may need to be treated in the hospital. Ask your metabolic doctor if you should carry a special travel letter with medical instructions for your child's care.

What happens when GA-1 is treated?

With prompt and lifelong treatment, children with GA-1 can often live healthy lives with typical growth and learning. Early treatment can help prevent episodes of metabolic crisis and the resulting health effects.

Even with treatment, some children continue to have episodes of metabolic crisis. This can lead to brain damage and long-term problems with involuntary movements and spasticity. After age six, metabolic crises are less common.

What causes the glutaryl-CoA dehydrogenase enzyme to be absent or not working correctly?

Genes tell the body to make various enzymes. People with GA-1 have a pair of genes that do not work correctly. Because of the changes in this pair of genes, the glutaryl-CoA dehydrogenase enzyme either does not work properly or is not made at all.

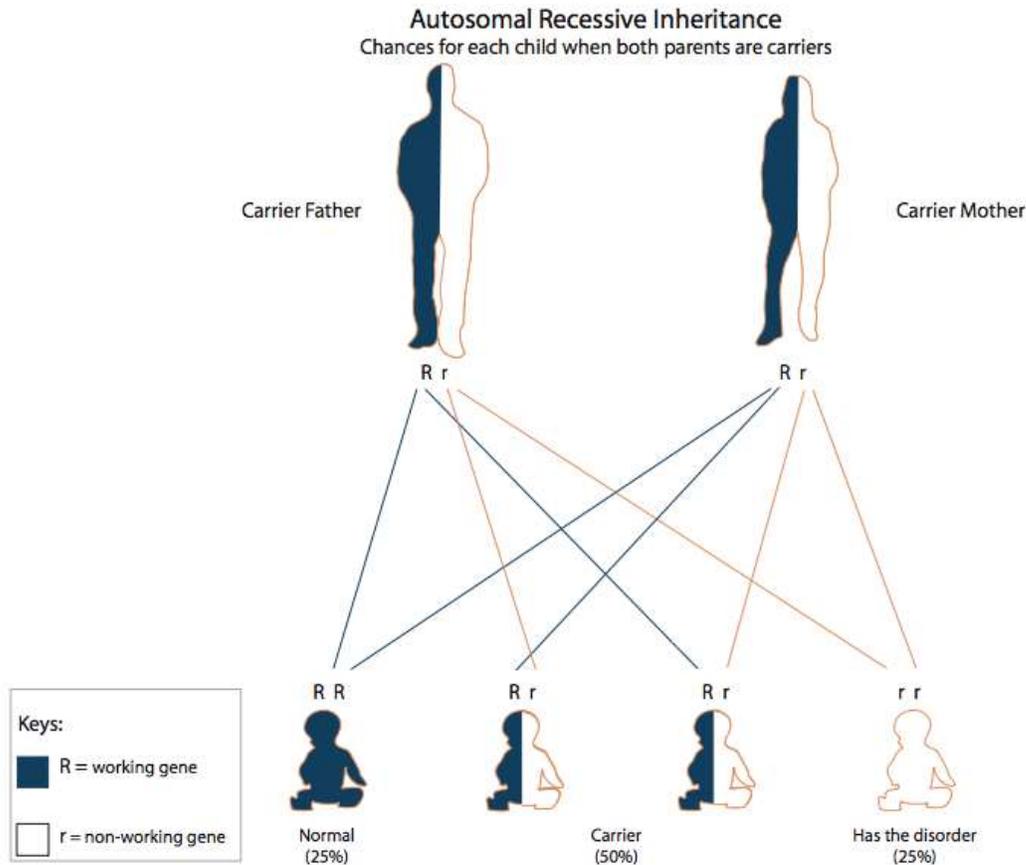
How is GA-1 inherited?

GA-1 is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has a pair of genes that make the glutaryl-CoA dehydrogenase enzyme. In children with GA-1, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent.

Parents of children with GA-1 rarely have the condition themselves. Instead, each parent has a single non-working gene for GA-1. They are called carriers. Carriers do not have GA-1 because the other gene of this pair is working correctly.

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have GA-1. There is a 50% chance for the child to be a carrier, just like the parents. And, there is a 25% chance for the child to have two working genes.



Genetic counseling is available to families who have children with GA-1. Genetic counselors can answer your questions about how the condition is inherited, choices during future pregnancies, and how to test other family members. Ask your doctor about a referral to a genetic counselor.

Is genetic testing available?

Genetic testing for GA-1 can be done on a blood sample. Genetic testing, also called DNA testing, looks for changes in the pair of genes that cause GA-1.

DNA testing is not necessary to diagnose your child. It can be helpful for carrier or prenatal testing, discussed below.

What other testing is available?

Special tests on blood, urine, or skin samples can be done to confirm GA-1. Talk to your metabolic doctor or genetic counselor if you have questions about testing for GA-1.

Can you test during pregnancy?

If both gene changes have been found in your child, DNA testing can be done during future pregnancies. The sample needed for this test is obtained by either CVS or amniocentesis.

Parents may choose to have testing during pregnancy or wait until birth to have the baby tested. A genetic counselor can talk to you about your choices and answer questions about prenatal testing or testing your baby after birth.

Can other members of the family have GA-1 or be carriers?

Having GA-1

The brothers and sisters of a baby with GA-1 have a chance of being affected, even if they haven't had symptoms. Finding out whether other children in the family have GA-1 is important because early treatment may prevent serious health problems. Talk to your metabolic doctor or genetic counselor about testing your other children.

GA-1 carriers

Brothers and sisters who do not have GA-1 still have a chance to be carriers like their parents. Except in special cases, carrier testing should only be done in people over 18 years of age.

Each of the parents' brothers and sisters has a 50% chance to be a carrier. It is important for other family members to be told that they could be carriers. There is a small chance they are also at risk to have children with GA-1.

All states offer newborn screening for GA-1. However, when both parents are carriers, newborn screening results are not sufficient to rule out GA-1 in a newborn baby. In this case, special diagnostic testing should be done in addition to newborn screening.

Can other family members be tested?

Diagnostic testing

Brothers and sisters of a child with GA-1 can be tested using blood, urine or skin samples.

Carrier testing

If both gene changes have been found in your child, other family members can have DNA testing to see if they are carriers.

If DNA testing would not be helpful, other methods of carrier testing may be available. Your metabolic doctor or genetic counselor can answer your questions about carrier testing.

How many people have GA-1?

About one in every 40,000 white babies in the United States is born with GA-1.

Does GA-1 happen more frequently in a certain ethnic group?

GA-1 occurs in people from all parts of the world. It is more common in people of Amish background in the United States, the Ojibway Indian population in Canada, and people of Swedish ancestry.

Does GA-1 go by any other names?

GA-1 is sometimes also called:

- Glutaric aciduria type 1
- Glutaryl-CoA dehydrogenase deficiency
- Dicarboxylic aminoaciduria
- Glutarate-aspartate transport defect

Where can I find more information?

Organic Acidemia Association

<http://www.oaaneews.org>

CLIMB (Children Living with Inherited Metabolic Disorders)

<http://www.climb.org.uk>

Save Babies through Screening Foundation

<http://www.savebabies.org>

