

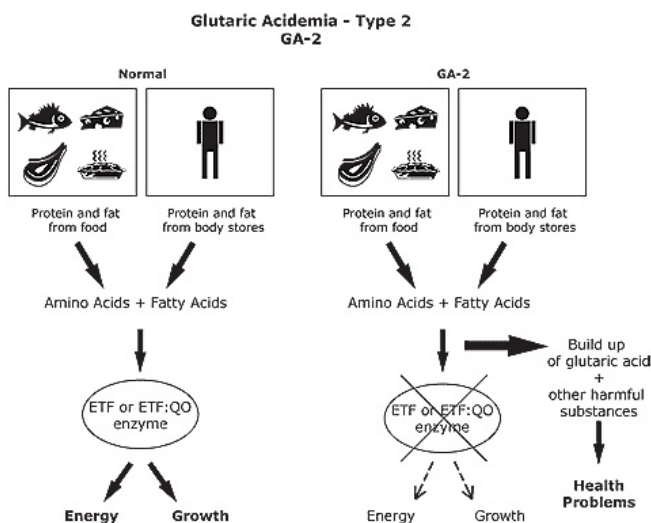


Glutaric aciduria Type II (GA-type II) A fact sheet for parents/carers

What is Glutaric aciduria type II (GA-2)?

GA-2 stands for “glutaric acidemia, type 2”. People with GA-2 have problems breaking down fat and protein into energy for the body. GA-2 has symptoms that are part of two different groups of disorders: fatty acid oxidation disorders and organic acid disorders.

What causes Glutaric aciduria type II (GA-2)?



GA-2 occurs when one of two different enzymes is either missing or not working properly. The enzymes responsible for GA-2 are called “electron transfer flavoprotein” (ETF) and “ETF-ubiquinone oxidoreductase” (ETF:QO). The job of these enzymes is to help make energy for the body by breaking down certain fats and proteins from the food we eat. They also break down fat and protein already stored in the body.

Energy from fat and protein keeps us going whenever our body runs low of its main source of energy, a type of sugar called glucose. Our bodies rely mainly on fat when we don't

eat for a stretch of time – like when we miss a meal or when we sleep. When either one of these two enzymes is missing, the body cannot break down protein and fat for energy, and must rely on glucose. While glucose is a good source of energy, there is a limited amount available. Once the glucose has been used up, the body tries to use fat and protein with limited success. This leads to the build up of glutaric acid and other harmful substances in the blood. It also causes low blood sugar, called hypoglycemia.

If Glutaric aciduria type II (GA-2) is not treated, what problems occur?

GA-2 can cause bouts of illness called metabolic crises. Some of the first symptoms of a metabolic crisis are:

- extreme sleepiness
- behavior changes
- irritable mood
- muscle weakness
- poor appetite

Other symptoms then follow:

- fever





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- nausea
- diarrhea
- vomiting
- hypoglycemia
- increased levels of acidic substances in the blood, called metabolic acidosis

If a metabolic crisis is not treated, a child with GA-2 can develop:

- breathing problems
- seizures
- coma, sometimes leading to death

Symptoms can first show up in the newborn period or later in childhood or sometimes even adulthood.

GA-2 in newborns

Some babies have their first symptoms shortly after birth. Rapid breathing and weak muscle tone often happen one to two days after birth. Episodes of metabolic crisis often show up at this time, too. Many babies with GA-2 have an odor that smells like “sweaty feet”. In addition, they often have serious heart and liver problems. Without treatment, most babies die within the first few weeks of life. Even with treatment, many babies with GA-2 die of severe heart problems within a few months. Some newborns with GA-2 also have birth defects. If this is the case, treatment is usually not helpful. Babies with GA-2 and birth defects usually die within the first weeks of life.

GA-2 in childhood

The symptoms of GA-2 can be very different from person to person. If symptoms do not happen in the newborn period, they may begin anytime from early childhood through adulthood.

Symptoms in childhood can include:

- nausea
- vomiting
- muscle weakness
- periods of hypoglycemia
- full metabolic crisis (described above)

Hypoglycemia can cause a child to feel weak, shaky or dizzy with clammy, cold skin. Hypoglycemia can occur:

- after strenuous exercise
- after eating too much protein
- after going too long without food
- during illness or infection

Episodes of metabolic crisis can happen for the same reasons.



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Other symptoms of GA-2 happen in some people:

- liver problems
- heart problems
- low levels of carnitine, a substance that helps the body use fat for energy
- involuntary movements

Some people with GA-2 never have symptoms and are only found to be affected after a brother or sister is diagnosed.

What is the treatment for Glutaric aciduria type II (GA-2)?

Your child's primary doctor will work with a metabolic doctor and dietician familiar with GA-2 to provide your child with medical care. Certain treatments may be advised for some children but not others. When necessary, treatment is usually needed throughout life. The following are treatments often recommended for children with GA-2:

1. Avoid going a long time without food

Infants and young children with GA-2 need to eat frequently to prevent hypoglycemia or 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 teens and adults with GA-2 can go without food for up to 12 hours without problems. They may need to continue the other treatments throughout life.

2. Diet

A low-fat, low-protein, high-carbohydrate diet is often advised. Carbohydrates give the body many types of sugar that can be used as energy. In fact, for children needing this treatment, most food in the diet should be carbohydrates (bread, cereal, pasta, fruit, vegetables, etc.). Do not remove all fat and protein from the diet. Children with GA-2 need a certain amount of each to grow properly. Your dietician can help you create a food plan that meets your child's needs. Any diet changes should be made under the guidance of a dietician experienced with GA-2.

3. Riboflavin, L-carnitine and glycine supplements

Some children and adults with GA-2 are helped by taking daily riboflavin supplements. Check with your doctor to see whether your child should take riboflavin. Some children





may be helped by taking 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. Some people with GA-2 are helped by taking glycine supplements. Ask your doctor whether your child should take glycine. Do not use any of these supplements without checking with your doctor.

4. Call your doctor at the start of any illness

Always call your health care provider when your child has any of the following:

1. poor appetite
2. low energy or extreme sleepiness
3. vomiting
4. diarrhea
5. an infection
6. a fever

During illness or infection, children with GA-2 have a much higher chance of developing hypoglycemia or a metabolic crisis. They need to drink fluids and eat extra carbohydrates when they are ill – even if they aren't 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 hypoglycemia or 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 Glutaric aciduria type II (GA-2) is treated?

GA-2 in newborns

A small number of newborns with symptoms of GA-2 have shown benefit from treatment. But, in most cases, treatment has not been helpful. Many newborns with GA-2 die from heart problems within the first few months of life.

GA-2 in children

With prompt and careful treatment, children and adults with GA-2 usually live healthy lives with normal growth and development. The goal of treatment is to prevent long-term problems. However, children who have repeated metabolic crises may develop life-long learning problems.

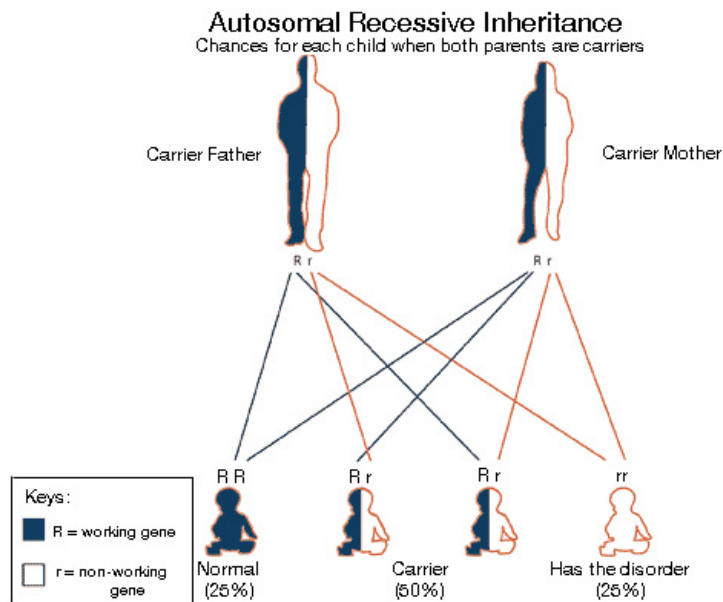
What causes the enzyme to be absent or not working correctly?

Genes tell the body to make various enzymes. People with GA-2 have a pair of genes that do not work correctly. Because of the gene changes, one of the necessary enzymes does not work properly or is not made at all.





How is Glutaric aciduria type II (GA-2) inherited?



GA-2 is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has one pair of genes that make the ETF enzyme and another pair that makes the ETF:QO enzyme. In children with GA-2, the pair of genes for one of these enzymes does not work correctly. These children inherit one non-working gene for the condition from each parent.

Parents of children with GA-2 rarely have the disorder. Instead, each parent has a single non-working gene for GA-2. They are called carriers. Carriers do not have GA-2 deficiency 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-2. 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-2. 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.

What other testing is available?

GA-2 can be confirmed by tests done on urine, blood or skin samples. Ask your metabolic doctor or genetic counselor about testing for GA-2.

Can other members of the family have Glutaric aciduria type II (GA-2) or be carriers?

Having GA-2

The brothers and sisters of a baby with GA-2 have a chance of being affected, even if they haven't shown symptoms. Finding out if other children in the family have GA-2 is important because early treatment may prevent serious health problems. Talk to your metabolic doctor or genetic counselor about testing your other children for GA-2.

GA-2 carriers

Brothers and sisters who do not have GA-2 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 GA-2 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-2. Some states do not provide newborn screening for GA-2. However, expanded newborn screening through private labs is available for babies born in states that do not screen for this condition. To learn more about expanded newborn screening, see How to obtain MS/MS. When both parents are carriers, newborn screening results are not sufficient to rule out GA-2 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

GA-2 can be confirmed by special tests using urine, blood, or skin samples.

How many people have Glutaric aciduria type II (GA-2)?

GA-2 is very rare. The actual incidence is unknown.

Does Glutaric aciduria type II (GA-2) happen more often in a certain ethnic group?

GA-2 does not happen more often in any specific race, ethnic group, geographical area or country.

Where can I find more information?

Fatty Oxidation Disorders (FOD) Family Support Group

<http://www.fodsupport.org>

Organic Acidemia Association

<http://www.oaanews.org>

United Mitochondrial Disease Foundation

<http://www.umdf.org>

CLIMB (Children Living with Inherited Metabolic Disorders)

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

Genetic Alliance

<http://www.geneticalliance.org/>

PacNoRGG pamphlet: Glutaric Acidemia Type II

http://mchneighborhood.ichp.edu/pacnorgg/media/Metabolic/glut_acid_eng.pdf

