



GA-2 **(Glutaric Acidemia, Type 2)**

What is it?

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 it?

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 enzymes is missing, the body cannot break down protein and fat for energy and 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 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:

- 1) Extreme sleepiness.
- 2) Behavior changes.
- 3) Irritable mood.
- 4) Muscle weakness.
- 5) Poor appetite.

Other symptoms then follow:

- 1) Fever
- 2) Nausea
- 3) Diarrhea
- 4) Vomiting
- 5) Hypoglycemia (low blood sugar)
- 6) 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:

- 1) Breathing problems.
- 2) Seizures.
- 3) Coma, sometimes leading to death.

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

GA-2 in Newborns

Some babies have their first symptoms shortly after birth. Rapid breathing and weak muscle tone usually 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:

- 1) Nausea.
- 2) Vomiting.
- 3) Muscle weakness.
- 4) Periods of hypoglycemia (low blood sugar).
- 5) Full metabolic crisis (described above).

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

Hypoglycemia can occur:

- 1) After strenuous exercise.
- 2) After eating too much protein.
- 3) After going too long without food.
- 4) During illness or infection.

Episodes of metabolic crisis can happen for the same reasons.

Other symptoms of GA-2 happen in some people:

- 1) Liver problems
- 2) Heart problems
- 3) Low levels of carnitine, a substance that helps the body use fat for energy
- 4) Involuntary movements

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

What is the treatment for GA-2?

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

Certain treatments may be advised for some children but not others. When necessary, treatment usually is needed throughout life. The following are treatments often recommended for children with GA-2:

Avoid Going a Long Time Without Food

Young children with GA-2 need to eat often to prevent hypoglycemia or a metabolic crisis. Most children should not go without food for more than four to six hours. Some children may need to eat even more often than this.

When they are well, most 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.

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.

Riboflavin, L-Carnitine and Glycine Supplements

Some children and adults with GA-2 are helped by taking 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 the body cells make energy. It also helps the body get rid of harmful wastes. Your doctor will decide whether 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.

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 excessive 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 (low blood sugar) or a metabolic crisis. When they are ill, they need to drink fluids and eat extra carbohydrates – even if they aren't hungry – or they could have a metabolic crisis.

Children who are sick often don't 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 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. Most 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 typical growth and development.

The goal of treatment is to prevent long-term problems. However, children who have repeated metabolic crises may develop lifelong 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.

Is GA-2 inherited?

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

Everyone has a 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 nonworking 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 because the other gene of this pair is working correctly.

When both parents are carriers, there is a 25 percent chance in each pregnancy for the child

to have GA-2. There is a 50 percent chance for the child to be a carrier, just like the parents. And, there is a 25 percent chance for the child to have two working genes.

Can other members of the family have 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 be done only in people over 18.

Each of the parents' brothers and sisters has a 50 percent 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.

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 for CTD

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

GA-2 Carrier Testing

Carrier testing for GA-2 may be available. Ask your metabolic doctor or genetic counselor whether carrier testing is possible for your family.

How may people have GA-2?

The incidence of GA-2 is unknown.

Does GA-2 happen more frequently in a certain ethnic group?

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

Does GA-2 go by any other names?

GA-2 is sometimes also called:

- 1) Glutaric acidemia-II.
- 2) Glutaric aciduria-II.
- 3) Multiple acyl-CoA dehydrogenase deficiency.
- 4) Electron transfer flavoprotein. dehydrogenase deficiency.
- 5) ETF/ETF QO deficiency.

Where can I find more information?

Fatty Oxidation Disorders (FOD) Family Support Group
www.fodsupport.org

Organic Acidemia Association
www.oaanews.org

United Mitochondrial Disease Foundation
www.umdf.org

Children Living with Inherited Metabolic Diseases (CLIMB)
www.climb.org.uk

Genetic Alliance
www.geneticalliance.org

Children's Special Health Services (CSHS)
State Capitol Judicial Wing
600 E. Boulevard Ave., Department 301
Bismarck, ND 58505-0269
Toll Free: 800.755.2714
701.328.2436
Relay TDD: 701.328.3975
CSHS website: www.ndhealth.gov/CSHS
North Dakota Department of Health website:
www.ndhealth.gov

Family support resources available from CSHS:

- Guidelines of Care Info
- Family Support Packet
- Financial Help Packet
- Insurance Fact Sheet

Family Resources

Family to Family Network
Center for Rural Health
University of North Dakota
School of Medicine and Health Sciences
P.O. Box 9037
Grand Forks, ND 58202-9037
Toll Free: 888.434.7436
701.777.2359
Fax: 701.777.2353
E-mail: NDF2F@medicine.nodak.edu
www.medicine.nodak.edu/crh

Pathfinder Services of ND
Pathfinder Family Center
1600 2nd Ave. SW, Ste. 19
Minot, ND 58701
Toll Free: 800.245.5840
701.837.7500
Relay TDD: 701.837.7501
E-mail: ndpath01@ndak.net
www.pathfinder.minot.com

Family Voices of North Dakota, Inc.
P.O. Box 163
Edgeley, ND 58433
Toll Free: 888.522.9654
701.493.2634
Fax: 701.493.2635
www.geocities.com/ndfv

**This fact sheet has general information.
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
should be followed by a metabolic doctor in
addition to their primary-care provider.

Acknowledgement

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