



Genetic Fact Sheets for Parents

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](http://www.newbornscreening.info)

Disorder name: Isovaleric Acidemia

Acronym: IVA

- What is IVA?
- What causes IVA?
- If IVA is not treated, what problems occur?
- What is the treatment for IVA?
- What happens when IVA is treated?
- What causes the isovaleryl-CoA dehydrogenase enzyme to be absent or not working correctly?
- How is IVA inherited?
- Is genetic testing available?
- What other testing is available?
- Can you test during a future pregnancy?
- Can other members of the family have IVA or be carriers?
- Can other family members be tested?
- How many people have IVA?
- Does IVA happen more often in a certain ethnic group?
- Does IVA go by any other names?
- Where can I find more information?

This fact sheet contains general information about IVA. 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 IVA should be followed by a metabolic doctor in addition to their primary doctor.

What is IVA?

IVA stands for “isovaleric acidemia.” It is one type of organic acid disorder. People with IVA have problems breaking down an amino acid called leucine 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.

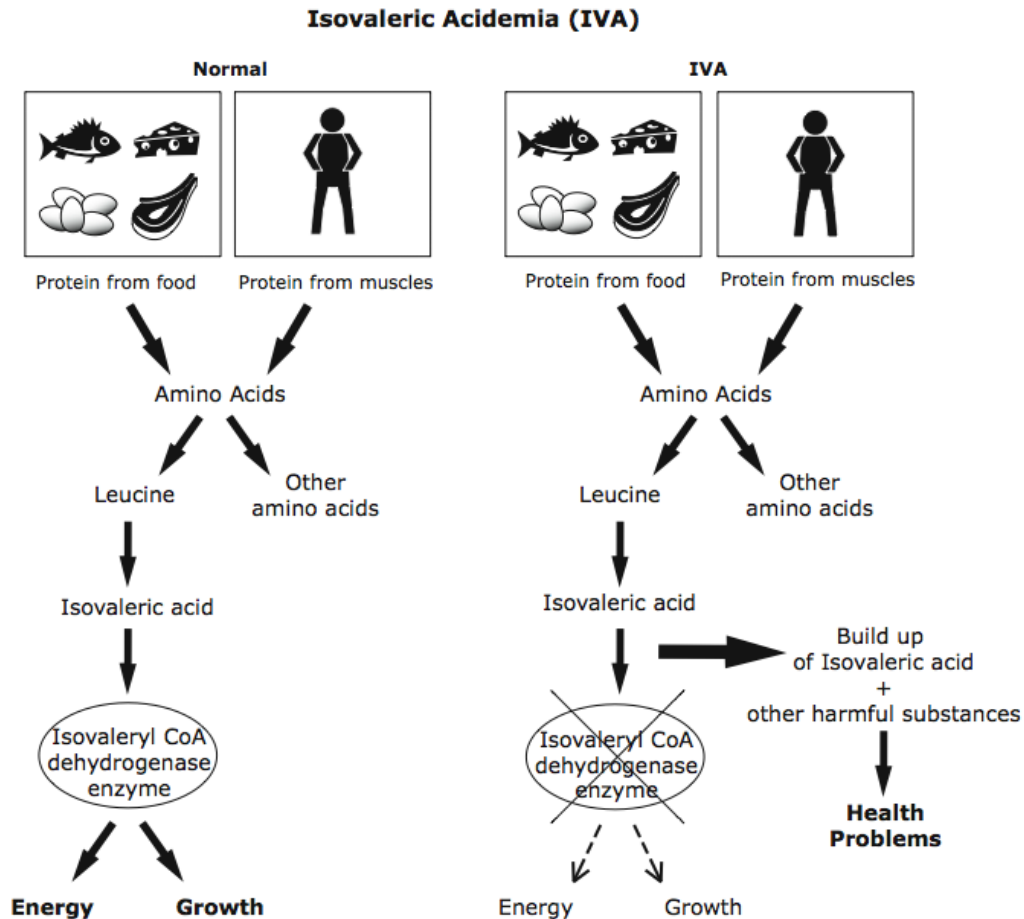
The symptoms and treatment vary between different organic acid disorders. They can also vary from person to person with the same organic acid disorder. See the fact sheets for each specific organic acid disorder.

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

What causes IVA?

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.

IVA occurs when an enzyme called “isovaleryl-CoA dehydrogenase” (IVD) is either missing or not working properly. This enzyme’s job is to help break down a substance called “isovaleryl-CoA.” It is made in the body when the amino acid leucine is broken down. When a child with IVA eats food containing leucine, the substance called isovaleric acid builds up in the blood and causes problems. Leucine is found in all foods that contain protein.



If IVA is not treated, what problems occur?

The effects of IVA vary from person to person. There are two main types of IVA. About half of all babies start showing symptoms shortly after birth. The other type called “chronic-intermittent,” starts later in infancy or childhood.

IVA in babies

Babies with IVA seem healthy at birth. Often, the first symptoms start between one day and two weeks of age.

IVA causes episodes of illness called metabolic crises. Some of the first symptoms of a metabolic crisis are:

- poor appetite
- extreme sleepiness or lack of energy
- vomiting
- problems staying warm
- an odor similar to “sweaty feet”

Other symptoms can then follow:

- increased levels of acidic substances in the blood, called metabolic acidosis
- high levels of ammonia in the blood
- ketones in the urine
- low platelets
- low level of white blood cells
- seizures
- swelling of the brain
- bleeding in the brain
- coma, sometimes leading to death

If not treated, many babies die during their first metabolic crisis. In those who survive, repeated episodes of metabolic crisis can cause brain damage. This can result in life-long learning problems or intellectual disabilities.

Chronic/intermittent IVA

Symptoms often start around one year of age. Some children, though, do not have symptoms until later in childhood.

Episodes of metabolic crisis can be brought on by illness, infection, or by eating large amounts of protein. When a child is ill, body protein is broken down for energy. In a child with IVA, this can cause high levels of isovaleric acid and results in a metabolic crisis.

Between episodes of metabolic crisis, children with IVA are usually healthy.

Some people have very mild or no symptoms and are only found to be affected after a brother or sister is diagnosed. Newborn screening also identifies infants that may never develop serious symptoms.

What is the treatment for IVA?

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

Prompt treatment is needed to prevent metabolic crises and the health effects that follow. You should start treatment as soon as you know your child has IVA. 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 IVA:

1. Low-leucine diet, medical foods, and formula

Most children need to eat a diet made up of foods low in leucine. Special medical foods and a leucine-free formula are usually part of the diet. Your dietician will create a food plan that contains the right amount of protein, nutrients, and energy to keep your child healthy. A special food plan should be continued throughout life.

Low-leucine / low-protein diet

Foods high in protein (and leucine) that may need to be avoided or limited include:

- milk and dairy products
- meat and poultry
- fish
- eggs
- dried beans and legumes
- nuts and peanut butter

Eating large amounts of these foods can cause isovaleric acid levels to rise, causing illness.

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

Do not remove all protein from the diet. Children with IVA need a certain amount to grow properly. Any diet changes should be under the guidance of a dietician.

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. Your dietician will tell you how to use these foods to supplement your child's diet.

In addition to a low-protein diet, many children are given a special leucine-free medical formula. Your metabolic doctor and dietician will decide whether your child needs this formula. Some states offer help with payment for this formula and others require private insurance to pay for the formula and other special medical foods.

2. Medications

Glycine is an amino acid that helps the body get rid of isovaleric acid. It is often given as a supplement to children with IVA. It may help prevent metabolic crises. Your doctor will tell you whether your child needs glycine and how much to use.

Some children may benefit 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 isovaleric acid and other harmful wastes. Your doctor will decide whether or not your child needs L-carnitine. Unless you are advised otherwise, use only L-

carnitine prescribed by your doctor. Do not use any medication or supplement without checking with your metabolic doctor.

Children with symptoms of a metabolic crisis need medical treatment right away. They may need to be treated in the hospital. During a metabolic crisis, children may be given bicarbonate, glucose, and other medications by IV to help reduce the acid levels in the blood.

3. Call your doctor at the start of any illness

In some children, even minor illnesses such as a cold or the flu 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
- vomiting
- diarrhea
- infection or illness
- fever

Children with IVA 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. In addition, they need to avoid eating protein when they are ill.

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 IVA is treated?

With prompt and careful treatment, children with IVA have a good chance to live healthy lives with typical growth and development.

Even when treated, some children still have repeated bouts of metabolic crisis. This can lead to life-long learning problems or intellectual disabilities. As they get older, children tend to have fewer metabolic crises.

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

Genes tell the body how to make enzymes. The IVD gene instructs the body to make the isovaleryl-CoA dehydrogenase (IVD) enzyme. Everyone has two copies of the IVD gene. People with IVA have changes, also called variants, in both copies of their IVD genes that cause them to not work correctly. Because of the variants in the IVD genes, the IVD enzyme either does not work properly or is not made at all.

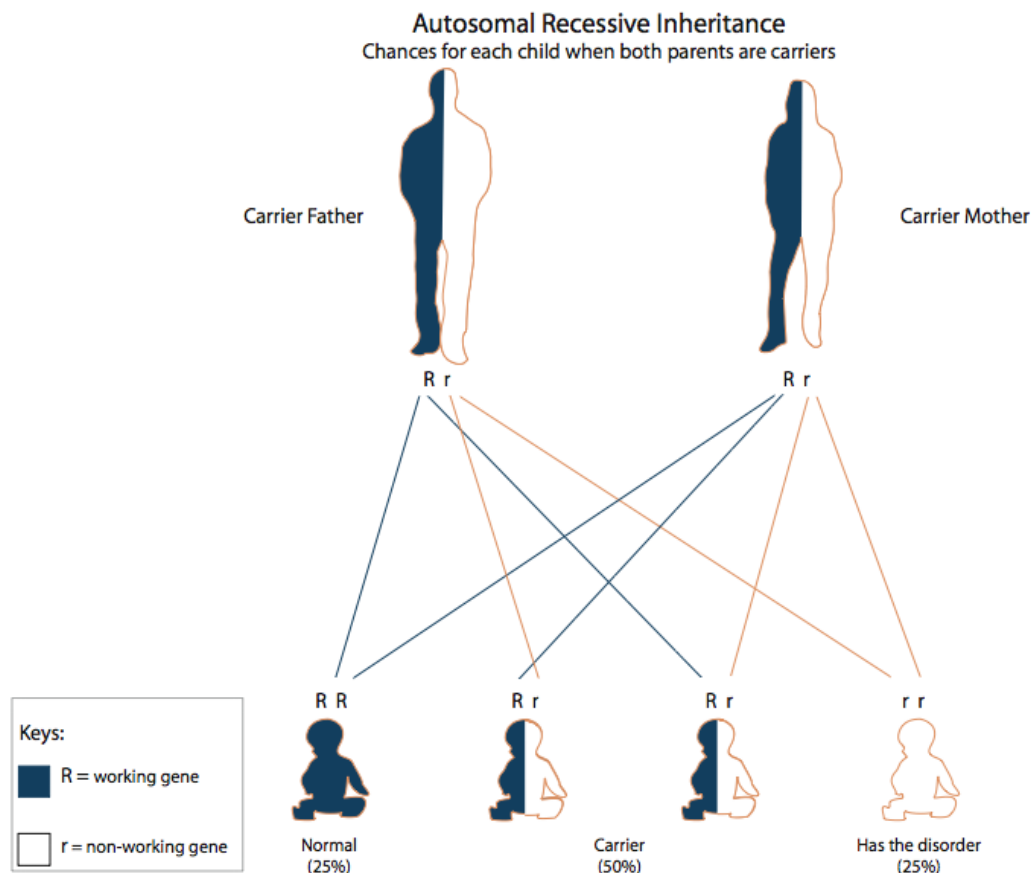
How is IVA inherited?

IVA is inherited in an autosomal recessive manner. It affects both boys and girls equally.

Everyone has two copies of the IVD genes that make the isovaleryl-CoA dehydrogenase enzyme. In children with IVA, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent.

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

When both parents are carriers, there is a 25% chance in each pregnancy for the child to have IVA. 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 IVA. 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 IVA can be done on a blood sample. Genetic testing, also called DNA testing, looks for changes (variants) in the IVD genes that causes IVA. If you have questions about DNA testing, talk with your genetic counselor or metabolic doctor.

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

What other testing is available?

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

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. Parents may also choose to use assisted reproductive techniques to decrease the chance that their future children would have IVA. 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 IVA or be carriers?

Having IVA

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

IVA carriers

Brothers and sisters who do not have IVA 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.

If you are a parent of a child with IVA, your brothers and sisters have 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 IVA.

All states offer newborn screening for IVA. However, when both parents are carriers, newborn screening results are not sufficient to rule out the condition 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 IVA can be tested using blood, urine, or skin samples.

Carrier testing

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

If DNA testing is not possible or 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 IVA?

About one in every 230,000 babies in the United States is born with IVA.

Does IVA happen more often in a certain ethnic group?

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

Does IVA go by any other names?

IVA is sometimes also called:

- isovaleric Acid CoA Dehydrogenase Deficiency
- IVD deficiency
- isovaleryl CoA carboxylase deficiency

Where can I find more information?

Organic Acidemia Association

<http://www.oaanews.org>

Metabolic Support UK

<https://www.metabolicsupportuk.org>

MedlinePlus

<https://medlineplus.gov/genetics/condition/isovaleric-acidemia/>

Baby's First Test

<http://www.babysfirsttest.org>

Isovaleric Acidemia: A Guide for Parents (PacNoRGG publication)

http://westernstatesgenetics.org/archives/pacnorgg/PDFs_all-081409/isovaleric_eng.pdf

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