

UNDERSTANDING ISOVALERIC ACIDEMIA

What is isovaleric acidemia?

Isovaleric acidemia is a genetic disorder that affects how protein is broken down in the body. It is a **metabolic** disorder.

Amino acids are the building blocks of protein. Normally, the protein we eat is broken down or "metabolized" in our bodies into amino acids and used for growth and tissue repair.

People who are born with isovaleric acidemia are unable to properly break down an amino acid called leucine in the food they eat. This is because they are missing an enzyme in their cells. Some people with isovaleric acidemia have a bit of this enzyme and some have none at all.

Enzymes can best be described as keys that unlock doors in the body. Think of the food in our system as a person with a big delivery to deliver. As long as the person has all the keys, the load can be delivered and everyone gets their packages. When enzymes or keys are missing, the packages cannot be delivered and the delivery person is left with a big load, and no one gets the packages they need to do their job.



Food eaten is like the delivery. In isovaleric acidemia, when the enzyme is missing, protein cannot be fully broken down for use by the body. It is only broken down to the 'acid' stage. This creates problems for the person with isovaleric acidemia. These acids build up in the blood, fluid around the brain and spinal cord, and urine. The name "isovaleric acidemia" means isovaleric acid in the blood. The acid is like the delivery person's packages. It cannot be delivered to the right place and the pile just keeps growing. When acids build up in the blood, they are like poison in the body. The person may not have an appetite, feel confused, not think clearly, sleep more than usual, or vomit. If the extra acid is not removed quickly, the person may have seizures or may go into a coma. A characteristic sign of isovaleric acidemia is the specific smell of sweaty feet during acute illness. This is caused by the buildup of isovaleric acid in the person's blood and body fluids.

In untreated isovaleric acidemia, the balance is upset between having enough protein (to meet body needs for growth and development) and having too much protein (which causes toxic levels of acid in the blood and body tissues). This imbalance is called **metabolic acidosis** and can cause:

- stunted growth
- developmental delay
- swelling around the brain
- brain damage
- seizures
- coma

Some people with isovaleric acidemia can have all of these complications and be severely affected whereas others may have only a few complications. It all depends on how much of the enzyme is working in their bodies and if their disorder is well-controlled.

How is isovaleric acidemia diagnosed?

Diagnosis is made by testing blood (acyl carnitine profile) and urine (urine organic acids) at a special genetic laboratory. These tests will show if the acids have built up in the blood and urine as a result of protein not being properly broken down.

How is isovaleric acidemia treated?

The treatment for isovaleric acidemia is aimed at preventing the buildup of acid in the blood. Therapy needs to begin before complications occur because, once they develop, they are irreversible. Treatment must be started as soon as the disorder is diagnosed.

The type of isovaleric acidemia determines the treatment. The following approaches are used alone or in combination.

DIET



People who have isovaleric acidemia and who have no working enzyme need to strictly follow a special diet to stay well.

The first part of treatment is **reducing protein in the diet**. If less protein is taken in, less acid will accumulate.



Protein in the diet is lowered by avoiding high protein foods like meat and milk. Examples of low protein foods are fruits, vegetables and starches. These foods provide calories without loading the body with excess protein.

Calories are a very important part of the diet. The body can use them for fuel without breaking down its own reserves. If the body does not have adequate fuel in the form of calories, it will actually begin to break down muscle to provide energy. Muscle is protein and will increase acid levels in the same way as eating protein will.

The metabolic dietitian works with people with isovaleric acidemia to make adjustments to diet. This ensures that adequate calories and nutrients are being provided. People with isovaleric acidemia may be asked to keep a record of what they eat on a daily basis for the dietitian to review and make diet recommendations.

The amount of food and drink the person can safely consume is calculated by the dietitian. All foods must be carefully measured to control the amount of protein consumed.

Examples of foods that must be eliminated from a low-protein diet are:

- milk and dairy products
- meat, fish, chicken
- nuts (including peanut butter)
- beans
- eggs

Eating high protein foods increases acid levels. This puts the person at risk of losing consciousness and having seizures.

It is not unusual for someone on a low-protein diet to have 2 kinds of vegetables and a baked potato for dinner. However, if these foods were all that the person ate, their diet would be lacking in protein, vitamins and minerals. That is where the special medical formula comes in. It provides all the protein and nutrients normally obtained from high-protein food. In order to prevent complications, the person must adhere to this diet for life.

The balancing act

The challenge in treating isovaleric acidemia is to provide enough protein to meet body requirements without overloading the person with protein waste (acid). Visits to the metabolic clinic are needed to consult with the team and make adjustments to food and medication. Regular blood work is necessary to monitor changes in blood levels and other nutritional indicators.

The delicate balance can be upset by strenuous exercise and illness. Both can cause the acid levels to rise. Extra calories are needed at these times to provide the stressed body with fuel.



MEDICATION

1. Carnitine

Carnitine is prescribed to people with isovaleric acidemia (IVA). Taking carnitine is important for people with the disorder for two reasons:

- People with IVA don't have enough carnitine in their bodies
- the low protein diet doesn't provide carnitine from natural sources

Carnitine also helps rid the body of toxic metabolites that build up in people with IVA. Carnitine is available in liquid or pill form.

2. Glycine

Glycine is an amino acid that acts like a sponge for the acids that build up in the blood of people with isovaleric acidemia. Glycine allows the acids to be safely eliminated in the urine.

How do people get isovaleric acidemia?

Isovaleric acidemia is an inborn error of metabolism. It is genetic. This means that the person has the disorder from the time they are conceived. At conception, the baby receives two sets of genetic material, one from the mother, and one from the father. This genetic material, called **DNA**, acts as a recipe for the baby's development.



DNA includes information about the baby's eye and hair colour, sex and even whether the baby will be right or left-handed. DNA comes in units called **genes**. Each pair of genes gives directions to a certain part of the body.

In isovaleric acidemia, there is a problem with one of the genes that give information on how the body breaks down protein. The disorder is caused by getting two copies of the faulty gene that gives the wrong instructions. One copy comes from the mother and one comes from the father. If the child inherits only one copy of the gene, they are a carrier for isovaleric acidemia but are not affected. There is a 1 in 4, or 25% chance that two carriers of the gene will have a baby with isovaleric acidemia. Boys and girls are equally affected.

With each pregnancy, there is the **same** 25% chance of having a child with isovaleric acidemia. In some families, there may be only one child with isovaleric acidemia, while in other families, multiple children may be affected.



For a person with isovaleric acidemia to have a baby with the same disease, they would need to have a partner who carried the gene. The chance of this would be very low as the gene mutation is rare.

How can family and friends help?

Learn to recognize the signs of trouble. If you know the person well, you will be the first to notice changes in behavior that suggest the acid levels are too high. For example, the person may become irritable, less active and sleep more than usual. Encourage the person to call the clinic.

Very high levels of acid in the blood may cause problems like:

- confusion
- vomiting
- increased sweating
- laboured breathing
- loss of consciousness
- seizures

If your friend or family member show any of the signs or symptoms of high acid levels or **metabolic acidosis**, take them to the emergency room immediately. The person with the isovaleric acidemia has a yellow wallet card with emergency room instructions and phone numbers.

Resources

Organic Acidemia Association

www.oaanews.org

Genetics Home Reference

<http://ghr.nlm.nih.gov/condition/isovaleric-acidemia>
