
ISOVALERIC ACIDEMIA

A Guide for Parents



Sponsored by the
Pacific Northwest
Regional Genetics Group (PacNoRGG)

This booklet contains general information about isovaleric acidemia.

As every child with this disorder is different, the information in this booklet may not apply to your child specifically.

Please share this booklet with anyone who cares for your child, such as health providers, nutritionists, and other health care workers, school professionals, childcare providers, and members of your family.

Feel free to ask your child's health provider any questions you may have about the enclosed information.

For your reference, a glossary of medical terms is included in the back of the booklet.

Isovaleric Acidemia

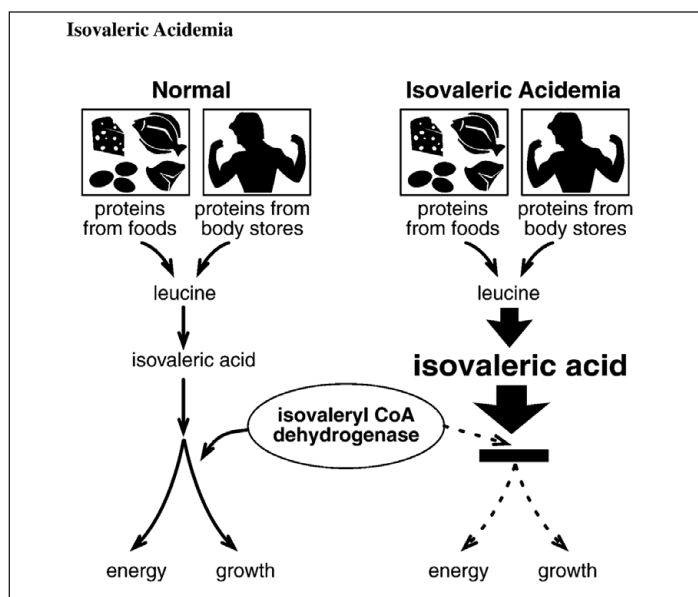
Isovaleric acidemia (pronounced i-so-val-are-ic a-sid-ee-mia) is a rare, inherited disorder. About 1 in every 100,000 babies born in the United States has isovaleric acidemia.

People with isovaleric acidemia have an enzyme (a substance that promotes chemical reactions) that does not work properly. Because of this, people with isovaleric acidemia cannot completely break down protein.

When foods high in protein, such as meat or eggs, are eaten, the protein is broken down by enzymes into many different substances. One of these substances is chemically changed to isovaleric acid (which is used by the body for growth and energy). If too much protein is eaten, more isovaleric acid is produced than the body can use. In order for the body to rid itself of excess isovaleric acid, an enzyme called isovaleryl-CoA dehydrogenase (i-so-val-are-il Co-A de-hi-drog-en-ase) is required. In people with isovaleric acidemia, because this enzyme doesn't work properly, levels of isovaleric acid build up and become harmful to the body.

To prevent this, children with isovaleric acidemia must follow a strict food pattern (another term for diet) which limits protein in order to stay healthy. (See Diagram 1.)

Diagram 1. The metabolic defect in isovaleric acidemia.



Protein eventually gets broken down to leucine (as well as many other amino acids) and then to isovaleric acid. Because the enzyme isovaleryl CoA dehydrogenase is inactive, isovaleric acid does not get completely broken down. The acid build-up results in illness.

Symptoms of Isovaleric Acidemia

It is important to remember that all children are unique and will be affected by this disorder to varying degrees. Some children will display symptoms that other children will not.

When isovaleric acidemia is untreated, isovaleric acid accumulates in the blood and affects the brain and nervous system. Initial symptoms of high isovaleric acid blood levels include lack of appetite, vomiting, and tiredness. If isovaleric acid levels remain elevated, symptoms can progress to seizures, coma, and even death. Symptoms can be triggered by eating too much protein, or by illness. When a child is ill, the body breaks down protein stored in the body to use for everyday metabolic functions. Thus, when a child with isovaleric acid is sick, excess protein can be released into the body, leading to increased levels of isovaleric acid.

If isovaleric acid levels in the body stay high for too long, damage to the brain occurs. This damage results in developmental delay. The harmful effects of isovaleric acidemia can be prevented if a food pattern low in protein is started in infancy and continued throughout life. A low protein food pattern is the only way to keep isovaleric acid levels at a safe level. Then the brain can function normally and the child with isovaleric acidemia will learn, and grow.

Treatment

There are three parts to successful treatment of isovaleric acidemia:

1. A low protein food pattern and/or specialized medical food (formula).

The most effective treatment for isovaleric acidemia is a food pattern low in protein. This food pattern helps prevent build-up of isovaleric acid.

A special medical food (formula) may also be prescribed for your child. Medical foods supply protein without the amino acids which are not metabolized in isovaleric acidemia. However, these amino acids are required for growth so they are added back in small amounts as infant formula or cow's milk.

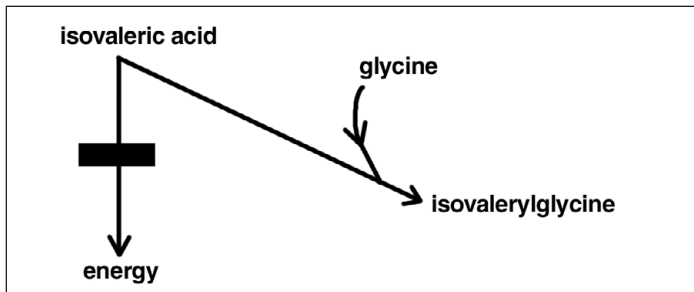
A low protein food pattern does not mean a protein-free food pattern. The body needs small amounts of protein to function properly. All children are different,

and as they grow, their needs change, so different amounts of protein can be tolerated. Frequent visits to the health provider and/or nutritionist are recommended to be sure a proper food pattern is prescribed.

2. Supplemental carnitine and glycine given by mouth.

Carnitine is essential for muscle energy production and also binds chemically with isovaleric acid to make it less harmful.

Diagram 2.



Since isovaleric acid cannot be broken down, the addition of glycine causes isovaleric acid to convert to isovalerylglycine, which is less harmful to the body.

Glycine is an amino acid which combines with isovaleric acid, and transforms it into a less harmful compound called isovalerylglycine. Isovalerylglycine can be safely excreted in the urine. This means that glycine provides a safe and efficient way of removing extra isovaleric acid so it won't accumulate and cause harm. (See Diagram 2.)

Discuss your child's treatment options with your health provider. The use of these supplements varies with the needs of each individual child.

3. Immediate contact with your child's health provider when illness occurs.

All children become ill at times, whether or not they have isovaleric acidemia. Sometimes they catch a cold, the flu, or something more severe. Your child with isovaleric acidemia will need to take special precautions during these times. Typical childhood illnesses can cause the body to break down its own protein, causing isovaleric acid to build up.

Give your child fluids and foods with extra energy, but no protein. Extra energy foods, such as sugar, will decrease the amount of protein broken down by the body. Feeding an ill child can sometimes be difficult, as sick children often have very little appetite. Encourage drinking of fluids as much as possible.

Many children enjoy drinks which are frozen, then chipped into ice chunks.

Always call your child's health provider when your child is vomiting, has diarrhea, has an infection, or has a fever of more than 101 degrees Fahrenheit.

Nutrition and Dietary Guidelines

The most effective treatment for isovaleric acidemia is a food pattern low in protein. High protein foods that should be limited include milk and dairy products, meat, fish, chicken, eggs, beans, peanut butter, and nuts.

Remember, it should be noted again that your child needs small amounts of protein for growth and development. Protein will not be completely eliminated from the food pattern. A nutritionist can help you create a specific food pattern to ensure your child will be well-nourished.

Many foods contain varying amounts of protein. Some foods should be eliminated entirely because they contain too much, while other foods may be eaten in moderate amounts, and still others may be eaten freely.

The Low Protein Food Pattern

A. Lower protein foods which can be included:

Medical foods (formula): If a medical food is needed, a prescribed amount of formula and a recipe for its preparation will be provided. This recipe may change frequently based on the child's growth, development, and blood levels.

Cereals and Grains (1/2 cup serving has about 2 grams of protein)

- | | |
|-----------------|-----------------|
| cold cereals | pita bread |
| hot cereals | tortillas |
| bagels | animal crackers |
| breads | graham crackers |
| pasta noodles | crackers |
| croutons | popcorn |
| English muffins | corn |
| rice | potatoes |
| rolls | lentils |
| buns | sweet potatoes |
| wheat germ | yams |

Vegetables: (1/2 cup serving has about 1 gram protein)

| | | |
|----------------------|------------------|-----------|
| broccoli | vegetable juices | mushrooms |
| green beans and peas | carrots | squash |
| asparagus | lettuce | spinach |
| cauliflower | cabbage | radishes |
| | onions | |

Fruits: (1/2 cup serving has a trace of protein)

| | | |
|----------------|--------------|------------|
| apples | berries | raisins |
| oranges | cherries | pineapples |
| fruit cocktail | peaches | kiwi |
| apricots | pears | tomatoes |
| grapes | fruit juices | |

B. High protein foods which should be avoided or used only in prescribed amounts:

(1 oz meat, 1 egg, or 8 oz milk each contain 7-10 grams protein)

| | | |
|---------------------------------|---------------|----------------------|
| meats | cheeses | dairy products |
| all forms of milk | fish | dried peas and beans |
| nuts, seeds, and their products | yogurt | ice cream |
| poultry | peanut butter | eggs |

C. Foods with NO protein which only provide extra energy

| | | |
|------------------|-----------|-------------------------------|
| gum drops | sugar | oils |
| hard candy | popsicles | suckers |
| Kool-aid | sodas | low protein pastas and breads |
| jams and jellies | margarine | |

You may have questions regarding the amounts of protein in each food, and the following books may be good references for you to have. Your nutritionist should be able to tell you how they can be purchased.

Low Protein Food List for PKU

by Virginia Schuett
Dietary Specialties, Inc
PO 227, Rochester, NY
800/544-0099

Bowes & Church's Food Values of Portions Commonly Used, 17th ed.

by Jean AT Pennington
JB Lippincott

Your nutritionist can recommend a wide variety of special low protein foods which can offer more food choices and add variety to your child's diet.

For infants and young children with isovaleric acidemia, a special liquid formula without added leucine (sometimes called a medical food) is often given to provide the nutrients needed for growth and development. Ask your health provider or nutritionist if this is needed.

Because your child will be limiting certain foods, the food pattern may not always contain enough vitamins and minerals. **A general multivitamin and mineral**

supplement that contains calcium and iron is essential.

Length of Treatment and Medical Visits

Isovaleric acidemia does not go away. The low protein food pattern must be continued throughout life to maintain health. Stopping the food pattern may lead to nervous system damage, no matter how old your child is. However, as your child matures and develops, larger amounts of protein may be tolerated. Your child's nutritionist will be able to modify the food pattern when necessary.

Because your child has a lifelong condition that could harm growth and development, your child should be followed closely by your health provider and nutritionist.

Medical visits offer many advantages for children with isovaleric acidemia. The medical team will want to learn how your child is getting along with parents, siblings, and friends, and work with you to solve problems. The goal is to help your child develop skills needed to take responsibility for managing his or her own condition. The staff knows this will be no easy task, and wants to provide as much support as they can to you and your family. Most importantly, these visits offer you an opportunity to ask questions and get answers.

At a medical visit, you and your child can expect any of the following:

| WHAT TO EXPECT: | HOW IT WILL HELP: |
|--|--|
| Discussion of medical history since last appointment | To determine if treatment is working, and to see if changes are needed; To talk about concerns at home, at school, with friends and/or with caregivers |
| Physical exam | To look at neurological status and other measures of physical well-being |
| Record of height, weight, and head size | To monitor child's growth and treatment |
| Food records | To look at food choices, assess the amounts of fats and proteins eaten, and adjust as needed |
| Developmental exam | To assess child's learning and development |
| Blood draw | To measure levels of amino acids and other compounds in the blood |

Organizing Your Information

You may want to buy a 3-ring notebook binder with tab dividers to record information, questions, and food patterns. Here you can collect treatment plans, growth and medication records, questions, articles, food lists, recipes, and other information that may be useful to you. One section might hold food records, and another a graph of your child's growth and development. Make a list of questions as you think of them, so you'll remember them at your next medical visit.

Social Concerns

Every child is different, and will be affected by isovaleric acidemia to a different degree. Some children will display physical or learning disabilities, while some may not. Your child will be tested periodically to assess these factors, and community resources are available to help you address the challenges of raising a child with special needs.

All family members play a very important role in your child's treatment. Other children in your family, as well as the child with isovaleric acidemia, should be taught about the low protein food pattern. Encourage all family members, including brothers and sisters, to help choose and prepare foods low in protein. Explain isovaleric acidemia to everyone who will participate in the care of your child (relatives, teachers, daycare providers, friends, baby-sitters, and others). They must understand the importance of the strict food pattern and become familiar with foods allowed and not allowed. Be sure to emphasize the importance of the special food pattern for growth and development. Also teach siblings and relatives not to feel sorry for the child with the disorder because he or she cannot eat certain foods.

Treat your child with isovaleric acidemia as normally as possible. Despite efforts to make your affected child feel good about himself or herself, there may come a time when your child becomes aware of his or her uniqueness and simply wants to be like everyone else. Help your child celebrate his or her individuality and realize that every person is different in some way.

Genetics

Within each child there are two copies of every gene; one copy from the mother and the other copy from the father. Most often, genes work normally. Sometimes however, a gene is changed from its original form. This

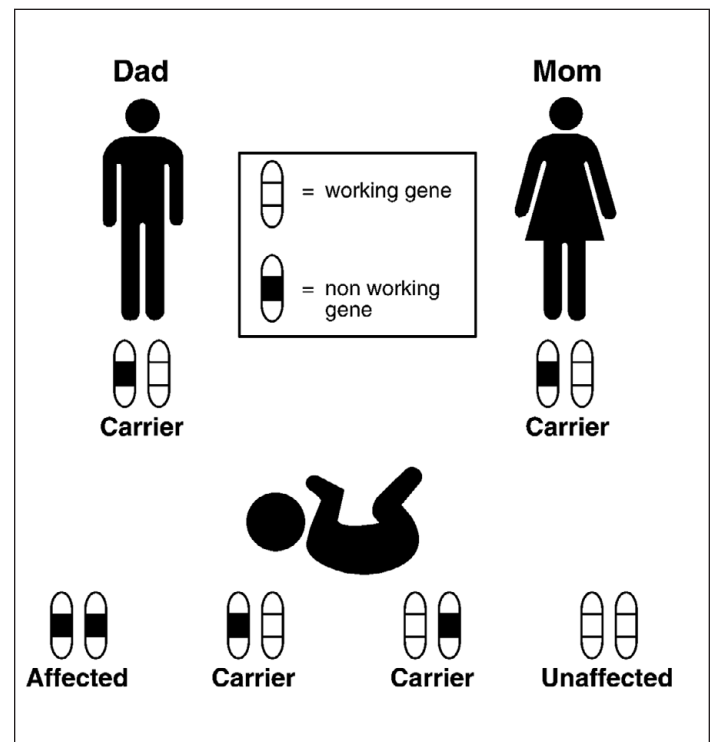
is called a mutation. Mutations usually cause genes not to work correctly.

The gene change that causes isovaleric acidemia is inherited in what is called an autosomal recessive pattern. This means that one copy of the changed, or non-working, gene must be inherited from each parent for a child to be affected with the disorder. The parents' health is not affected because their other copy of the gene is working correctly. Therefore, each parent is called a gene "carrier." It is important to remember that all people carry several of these "hidden" recessive genes. Also, it is no one's fault that your child was born with isovaleric acidemia, and both boys and girls can have the disorder.

The chance that two parents who carry the same changed gene will have a child with the disorder is one in four, or 25% with each pregnancy. The chance these parents will have a child that is healthy, but a carrier, is one in two, or 50% with each pregnancy. There is also a one in four, or 25% chance that these parents will have a child who is neither affected nor a carrier. (See Diagram 3.)

For affected individuals planning to have children, a consultation with a genetic counselor is recommended. The genetic counselor can explain the chances of any future children being affected with the disorder, and can also explain options for testing.

Diagram 3. Autosomal recessive inheritance



The chance that two parents who carry the same changed gene will have a child with the disorder is one in four, or 25% with each pregnancy.

Resources

Following is a list of agencies that may be helpful to you. Each agency specializes in different areas, such as health care, physical or mental development, support groups, or general information. Since each child is affected differently, not all agencies may be useful to you.

The ARC of the United States

National Headquarters Office
1010 Wayne Ave, Ste 650
Silver Spring, MD 20910
301/565-3842
Fax: 301/565-5342
info@thearc.org
http://www.TheArc.org

Genetic Alliance, Inc.

4301 Connecticut Ave NW Ste 404
Washington DC 20008
202/966-5557; 800/336-GENE (4363)
info@geneticalliance.org
http://www.geneticalliance.org

Metabolic Information Network

PO Box 670847
Dallas TX 75367-0847
214/696-2188; 800/945-2188
Fax: 214/696-3258
mizesg@ix.netcom.com

MUMS: National Parent-to-Parent Network

150 Custer Court
Green Bay Wisconsin 54301-1243
920/336-5333
Fax 920/339-0995
mums@netnet.net
http://www.netnet.net/mums

National Center for Learning Disabilities

381 Park Ave S Ste 1401
New York NY 10016
212/545-7510; 888/575-7373
Fax: 212/545-9665
http://www.nclد.org

National Parent Network on Disabilities (NPND)

1130 - 17th Street NW Ste 400
Washington DC 20036
202/463-2299
Fax: 202/463-9405
npnd@mindspring.com
http://www.npnd.org

National Society of Genetic Counselors

233 Canterbury Drive
Wallingford PA 19086-6617
610/872-7608
nsgc@aol.com
http://www.nsgc.org

NORD: National Organization for Rare Disorders

PO Box 8923
New Fairfield CT 06812
203/746-6518; 800/999-6673
Fax: 203/746-6481
orphan@rarediseases.org
http://www.rarediseases.org

Organic Acidemia Association

c/o Kathy Stagni
13210 - 35th Ave N
Plymouth MN 55441
763/559-1797
Fax: 763/694-0017
oanews@aol.com
http://www.oanews.org

Washington State Parent-to-Parent Program

4738 - 172nd Court SE
Bellevue WA 98006
425/641-7504; 800/821-5927
statep2p@earthlink.net
http://www.arcwa.org

ALASKA

PARENTS: Parents as Resources Engaged in Networking and Training

4743 Northern Lights
Anchorage AK 99508
907/337-7678
Fax: 907/337-7671
parents@parentsinc.org
http://www.parentsinc.org/

IDAHO

Idaho Parents Unlimited

4696 Overland Road Ste 568
Boise ID 83705
208/342-5884; 800/242-4785 (ID only)
Fax: 208/342-1408
ipul@rmci.net
http://home.rmci.net/ipul

MONTANA

PLUK: Parents, Let's Unite for Kids

516 N 32nd Street
Billings MT 59101
406/255-0540; 800/222-7585
Fax: 406/255-0523
plukinfo@pluk.org
http://www.pluk.org

OREGON

Coalition in Oregon for Parent Education (COPE)

999 Locust Street NE
Salem OR 97303
503/581-8156; 888/505-COPE (2673)
Fax: 503/391-0429
orcope@open.org
http://www.open.org/~orcope/index.htm

WASHINGTON

Washington PAVE

6316 S 12th
Tacoma WA 98465
253/565-2266; 800/572-7368 (WA only)
Fax: 253/566-8052
wapave9@washingtonpave.com
http://www.washingtonpave.org

Treatment Plan

Prescribed food pattern:

Vitamin and/or mineral supplement: _____

Specific foods to be avoided:

Medication _____ Dose _____ Schedule _____

Important names and phone numbers:

Health Care Provider:

Nutritionist:

Hospital:

Genetic Counselor:

To Schedule Clinic Appointments:

Public Health Nurse:

Remember

Raising a child with a rare metabolic disorder can be challenging and often confusing. Your health care providers are there to help you, and can answer the questions you will have along the way. Please do not hesitate to call upon them as you make the many changes necessary for successful treatment of your child's disorder.

Glossary

Acidosis - the build up of harmful acids in the body.

Amino acids - building blocks which combine to form proteins.

Carrier - a person who carries one non-working (mutated) gene in a pair of genes. Carriers do not have the disorder, they simply carry one mutation for it.

Carnitine - a non-toxic, natural chemical which helps decrease the harmful by-products of normal protein breakdown.

Enzyme - a substance in the body that enables chemical reactions.

Food pattern - another term for diet. A food pattern consists of foods and beverages to be included or avoided on a daily basis.

Gene - the smallest unit of hereditary material.

Genetics - the study of heredity.

Glycine - an amino acid which combines with isovaleric acid to make it less harmful.

Mutation - occurs when a gene is changed from its original form.

Protein - the building blocks of body tissues.

Scientific References:

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<http://mchneighborhood.ichp.edu/pacnorgg>

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