



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>

Disorder name: Propionic Acidemia

Acronym: PA

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

What is PA?

PA stands for “propionic acidemia”. It is one type of organic acid disorder. People with PA have problems breaking down and using certain amino acids 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.

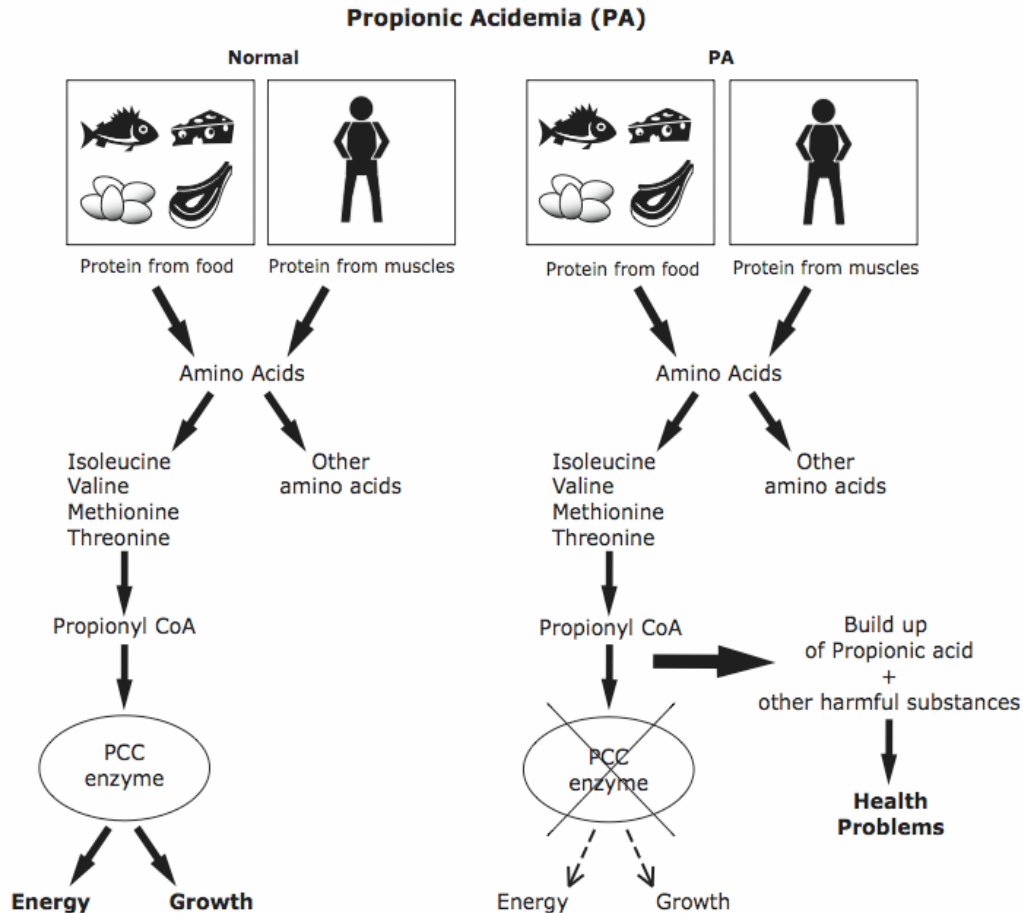
The symptoms and treatment vary between different organic acid disorders. They can also vary from person to person with the same organic acid disorder. See the fact sheets for each specific organic acid disorder.

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

What causes PA?

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.

PA occurs when an enzyme called “propionyl CoA carboxylase” (PCC) is either missing or not working properly. This enzyme’s job is to change certain amino acids so the body can use them. When this enzyme is not working, substances called glycine and propionic acid, along with other harmful substances, build up in the blood and cause problems.



The four amino acids that cannot be used correctly are isoleucine, valine, methionine, and threonine. These amino acids are found in all foods that contain protein. Large amounts are found in meat, eggs, milk and other dairy products. Smaller amounts are found in flour, cereal, and some vegetables and fruits.

If PA is not treated, what problems occur?

Each child with PA is likely to have somewhat different effects. Many babies with PA start having symptoms in the first few days of life. Others have their first symptoms sometime in infancy.

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

- poor appetite
- vomiting
- extreme sleepiness or lack of energy
- low muscle tone (floppy muscles and joints)

Common lab findings are:

- ketones in the urine
- high levels of acidic substances in the blood, called metabolic acidosis
- high blood ammonia levels
- high blood levels of glycine
- high levels of certain organic acids
- low platelets
- low white blood cells

If a metabolic crisis is not treated, a child with PA can develop:

- breathing problems
- seizures
- swelling of the brain
- stroke
- coma, sometimes leading to death

A metabolic crisis can be triggered by:

- eating large amounts of protein
- illness or infection
- going too long without food
- stressful events such as surgery

Between episodes of metabolic crisis, children with PA are often healthy.

Long-term effects are seen in some children with PA. These can include:

- learning disabilities or mental retardation
- delays in walking and motor skills
- abnormal involuntary movements (dystonia or choreoathetosis)
- rigid muscle tone, called spasticity
- poor growth with short stature
- seizures
- osteoporosis
- inflammation of the pancreas, called pancreatitis
- skin rashes

Without treatment, brain damage can occur. This can result in mental retardation. If not treated, many babies with PA die within the first year of life.

A small number of people with PA never show symptoms and are only found to be affected after a brother or sister is diagnosed.

What is the treatment for PA?

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

Prompt treatment is needed to prevent mental retardation and serious medical problems. Most children need to be on a low-protein diet and drink a special medical formula. You should start the diet and formula as soon as you know your child has PA.

The following are treatments often recommended for children with PA:

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

Low-protein diet

A food plan low in the amino acids leucine, valine, methionine, and threonine, with limited amounts protein is often recommended. Most food in the diet will be carbohydrates (bread, cereal, pasta, fruit, vegetables, etc.). Carbohydrates give the body many types of sugar that can be used as energy. Eating a diet high in carbohydrates and low in protein can help prevent metabolic crises.

Foods high in protein 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

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 PA need a certain amount of protein to grow properly.

Your dietician will create a food plan that contains the right amount of protein, nutrients, and energy to keep your child healthy. Your child will need to be on a special food plan throughout his or her life.

Medical formula and foods

In addition to a low-protein diet, your child may be given a special medical formula. This formula contains the correct amount of protein and nutrients needed for normal growth and development. Your metabolic doctor and dietician will tell you what type of formula is best and how much to use.

There are also 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 as part of your child's diet.

Some states offer help with payment, or require private insurance to pay for the formula and other special medical foods.

2. Avoid going a long time without food

Babies and young children with PA need to eat often to avoid a metabolic crisis. Most children should not go without food for more than 4 to 6 hours. Some children may need to eat even more often than this. It is important that babies be fed during the night. They may need to be woken up to eat if they do not wake up on their own.

You may be told to give your child a starchy snack before bed and another during the night. He or she may need another snack first thing in the morning. Raw cornstarch mixed with water, milk, or other drink is a good source of long-lasting energy. This is sometimes suggested for children older than one year of age. Your dietician can give you ideas for suitable snacks.

3. Medication

Children with PA may benefit by taking L-carnitine. This is a safe and natural substance that helps the body make energy. It also helps get rid of harmful wastes. L-carnitine is part of the usual treatment for PA. Your doctor will tell you how much your child needs. Unless you are advised otherwise, use only L-carnitine prescribed by your doctor.

Certain antibiotics, taken by mouth, can help reduce the amount of propionic acid in the intestines. Your doctor will decide if your child needs antibiotics and, if so, what type.

Some children may be given biotin supplements by mouth. Biotin is a type of B vitamin that helps the body make energy from food. Biotin has not been proven to help in PA. But, your doctor may talk with you about trying this supplement to see if it is of benefit to your child.

Children who are having symptoms of a metabolic crisis should be treated in the hospital. During a metabolic crisis, your child may be given medications such as bicarbonate by IV to help reduce the acid levels in the blood. Glucose is often given by IV to prevent the breakdown of protein and fat stored in the body.

Do not use any medication or supplement without first checking with your doctor or metabolic doctor.

4. Regular blood and urine tests

Tracking of ketones

Your child will have periodic urine tests to check the level of ketones. These can be done at home or at the doctor's office. Ketones are substances formed when body fat is broken down for energy. This can happen after going without food for

long periods of time, as the result of an illness, or during periods of heavy exercise. Ketones in the urine may signal the start of a metabolic crisis.

Blood tests

Your child will have regular blood tests to measure the levels of amino acids. Urine tests may also be done. Your child's diet and medication may need to be adjusted based on the results of these tests.

5. Call your doctor at the start of any illness

In children with PA, even minor illness 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 PA need to eat more starchy foods and drink more fluids when they are ill – even if they aren't hungry – or they could have a metabolic crisis. In addition, they should avoid eating protein during any illness.

Many children with PA need to be treated in the hospital during illness to avoid serious health problems. Ask your metabolic doctor if you should carry a special travel letter with medical instructions for your child's care.

What happens when PA is treated?

Babies who have prompt and ongoing treatment before they have a metabolic crisis may have normal growth and development. In general, the earlier treatment is started, the better the outcome.

Even with treatment, some children have life-long learning problems or mental retardation. Seizures or problems with involuntary movements also occur in some children, despite treatment. Children with PA often have more infections than usual. These need to be treated promptly to avoid a metabolic crisis.

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

Genes tell the body to make various enzymes. People with PA have a pair of genes that do not work correctly. Because of these gene changes, the PCC enzyme does not work properly or is not made at all.

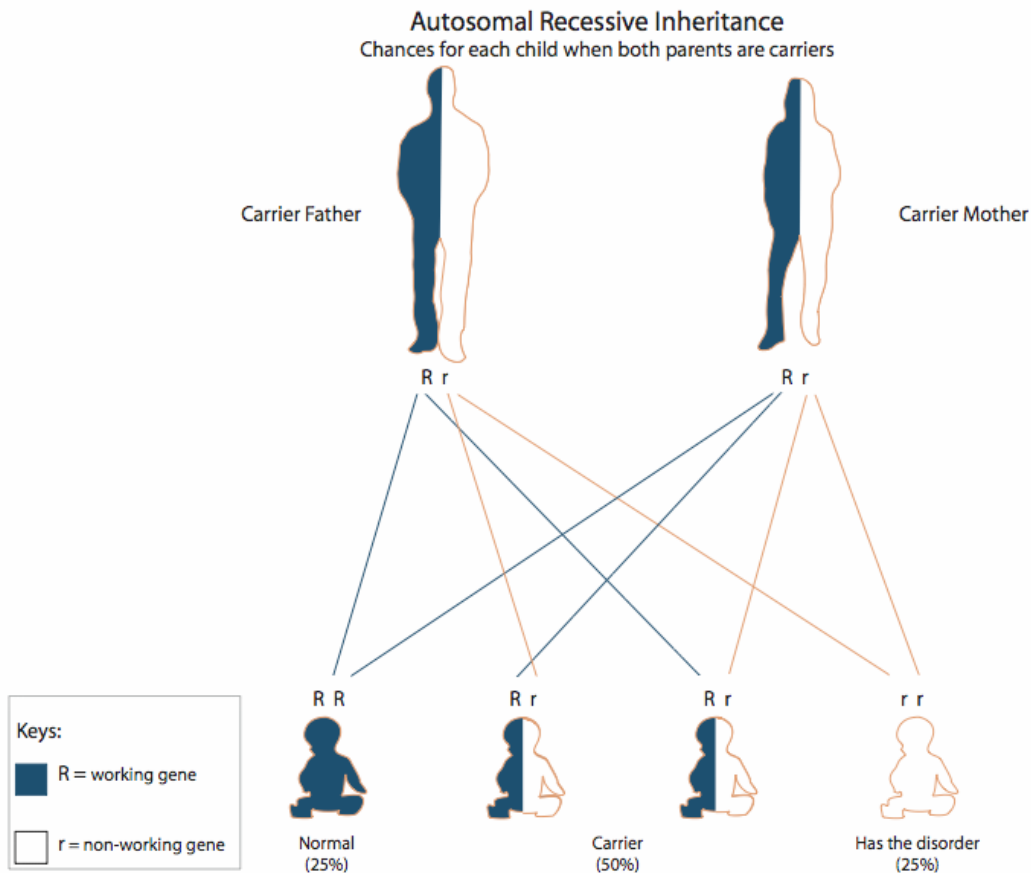
How is PA inherited?

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

Everyone has a pair of genes that make the PCC enzyme. In children with PA, neither of these genes works correctly. These children inherit one non-working gene for the condition from each parent.

Parents of children with PA rarely have the disorder themselves. Instead, each parent has a single non-working gene for PA. They are called carriers. Carriers do not have PA 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 PA. 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 PA. Genetic counselors can answer your questions about how PA 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 PA may be possible. Genetic testing, also called DNA testing, looks for changes in the pair of genes that causes PA. Talk with your genetic counselor or metabolic doctor if you have questions about DNA testing.

DNA testing is not necessary to diagnose your child. However, if it is available, 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 PA. Talk to your metabolic doctor or genetic counselor if you have questions about testing for PA.

Can you test during pregnancy?

If both gene changes have been found in your child with PA, DNA testing can be done during future pregnancies. The sample needed for this test is obtained by either CVS or amniocentesis.

PA can also be found through an enzyme test using cells from the fetus. The sample needed for this test is obtained by amniocentesis.

Parents may either choose to have testing during pregnancy or wait until birth to have the baby tested. 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 PA or be carriers?

Having PA

Older brothers and sisters of a baby with PA, if they are healthy and growing normally, are unlikely to have the condition. However, finding out if other children in the family have this condition may be important because treatment can prevent serious health problems. Ask your metabolic doctor or genetic counselor whether your other children should be tested.

PA carriers

Brothers and sister who do not have PA still have a chance to be carriers like their parents. Except in special cases, carrier testing should only be done on people over 18 years of age.

Each of the parents' brothers and sisters has a 50% chance to be a PA 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 PA.

Some states do not provide newborn screening for PA. 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 PA 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 PA can have special tests on blood, urine or skin samples. Talk to your doctor or genetic counselor if you have questions about testing for PA.

Carrier testing

Carrier testing for PA may be available. If you have questions about carrier testing, ask your genetic counselor or metabolic doctor.

How many people have PA?

About 1 in every 100,000 babies in the United States is born with PA.

Does PA happen more frequently in a certain ethnic group?

PA occurs in all ethnic groups around the world. It happens more often in the Arab population of Saudi Arabia. About one in 2000 to one in 5000 people of Saudi Arabian ancestry has PA.

Does PA go by any other names?

PA is sometimes also called:

- Propionyl-CoA carboxylase deficiency
- PCC deficiency
- Ketotic glycinemia
- Ketotic hyperglycinemia

Where can I find more information?

Propionic Acidemia Foundation
<http://www.pafoundation.com/pages/869028/>

Organic Acidemia Association
<http://www.oaanews.org>

CLIMB (Children Living with Inherited Metabolic Disorders)
<http://www.climb.org.uk>

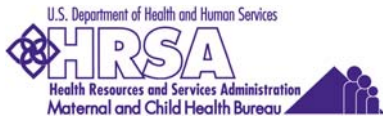
Save Babies Through Screening Foundation
<http://www.savebabies.org/>

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

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