



## Genetic Fact Sheets for Parents

# Amino 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: Homocystinuria

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

This fact sheet contains general information about homocystinuria. 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. Children with this condition should be followed by a metabolic doctor in addition to their primary care provider.

### What is homocystinuria?

It is one type of amino acid disorder. People with this condition have problems breaking down an amino acid called methionine from the food they eat.

### **Amino Acid Disorders:**

Amino acid disorders (AAs) are a group of rare inherited conditions. They are caused by enzymes that do not work properly.

Protein is made up of smaller building blocks called amino acids. A number of different enzymes are needed to process these amino acids for use by the body. Because of missing or non-working enzymes, people with amino acid disorders cannot process certain amino acids. These amino acids, along with other toxic substances, then build up in the body and cause problems.

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

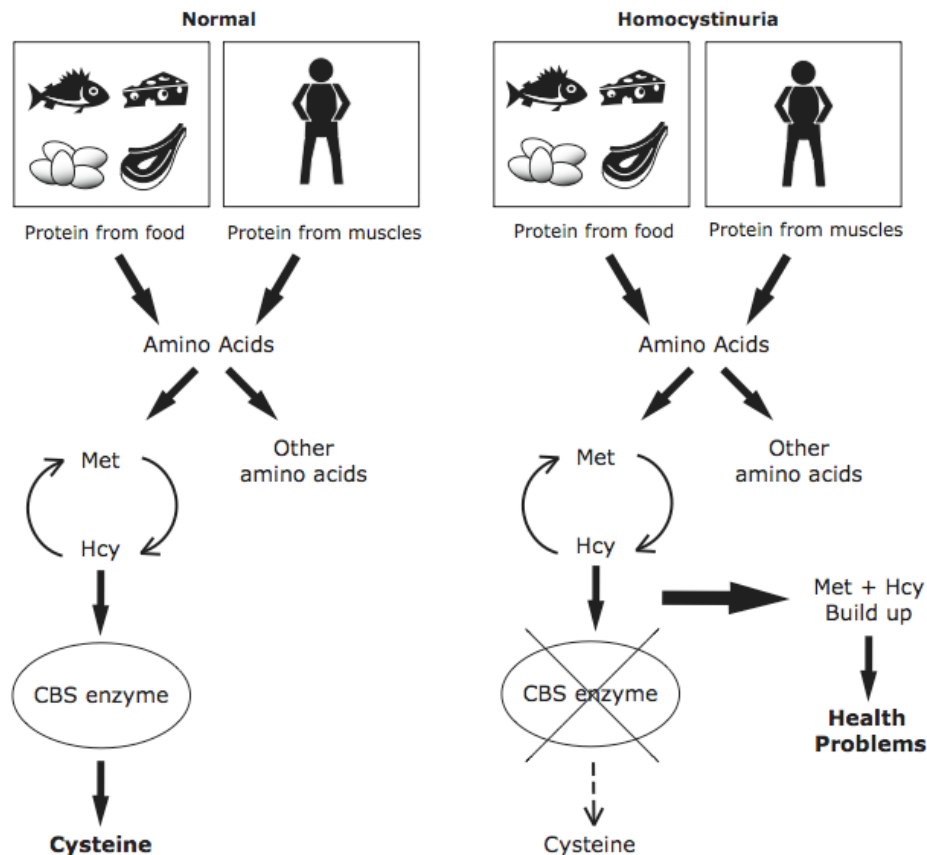
Amino acid disorders are inherited in an autosomal recessive manner and affect both males and females.

### **What causes homocystinuria?**

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.

This condition occurs when an enzyme called “cystathionine beta-synthase” (CBS) is either missing or not working properly. This enzyme’s job is to break down methionine. When the CBS enzyme is not working correctly, methionine and another amino acid, homocystine, build up in the blood and cause problems.

## HOMOCYSTEINURIA



### If homocystinuria is not treated, what problems occur?

Babies look healthy and normal at birth. Over time, if the condition is not treated, it can cause growth and learning delays. It can also affect the eyes, bones, heart, and blood vessels.

There are two types of homocystinuria. The milder form can be treated with vitamin B6 supplements. The other type does not respond to vitamin B6. Symptoms of both types vary widely from person to person.

#### **Growth, learning and behavior**

Delays in growth and learning are often noticed between the ages of one and three. Common effects in untreated children include:

- poor growth
- problems gaining weight
- delays in crawling, walking, and talking
- behavior and emotional problems
- serious learning disabilities or mental retardation

## **Eyes**

Children usually start to develop severe nearsightedness after one year of age. If this is not treated, the lens of the eye can become loose and move out of place. This is called "lens dislocation". This often happens between two and eight years of age. Glaucoma, a condition caused by increased eye pressure, can happen over time if the lens dislocation is not treated. Untreated glaucoma can cause blindness.

## **Bones and skeleton**

Teens and adults are often very tall and slender. They may have very long arms, legs, and fingers. By the teen-age years, about half have thinning of the bones, called osteoporosis.

Muscle weakness, especially in the legs, is a problem for some children.

## **Heart and blood vessels**

If not treated, homocystinuria can cause blood clots resulting in heart disease or stroke. In fact, stroke and heart disease are the main causes of early death in people with untreated homocystinuria.

## **Other**

Children who are not treated often have pale hair and skin. Some will have episodes of pancreatitis that causes severe pain.

## **What is the treatment for homocystinuria?**

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

Prompt treatment is needed to prevent mental retardation and other serious health problems. Most children need to eat a special diet low in methionine, drink a special formula, and take supplements every day. You should start the treatment as soon as you know your child has this condition. Lifelong treatment is usually needed to prevent or control the symptoms.

The following are treatments often recommended for children with homocystinuria:

### **1. Low-methionine diet:**

The special diet is made up of foods that are very low in methionine. This means your child must not have cow's milk, regular formula, meat, fish, cheese, or eggs. Regular flour, dried beans, nuts, and peanut butter also contain methionine and must be avoided or strictly limited.

Many vegetables and fruits have only small amounts of methionine and can be eaten in carefully measured amounts. There are other medical foods such as special low-protein or low-methionine flours, breads, and pastas that are made especially for people with homocystinuria.

Your metabolic doctor and dietician will decide on the best food plan for your child. Your child's diet will depend on many things such as his or her age, weight, and blood test results. Your dietician will fine-tune your child's diet over time. The diet is usually needed throughout life.

## **2. Medical Foods and Formula**

In addition to a low-methionine diet, some children are given a special medical formula as a substitute for milk. This formula will give your child the correct amount of nutrients and protein while helping to keep his or her methionine and homocystine levels within a safe range. Your metabolic doctor and dietician will tell you what type of formula is best for your child and how much to use.

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

## **3. Supplements**

### **Vitamin B6**

Some children are helped by vitamin B6 supplements. In children who benefit from this treatment, the supplements help prevent mental retardation and behavior problems. Vitamin B6 may also reduce the risk for blood clotting and eye and bone problems.

Ask your metabolic doctor whether your child would benefit from vitamin B6 supplements. Your doctor can do special tests to figure out whether your child will respond to vitamin B6.

### **Betaine**

Betaine is a vitamin-like substance found in grains and other foods. It can also be bought in pill form as a supplement. Betaine can help lower the amount of homocystine in the blood, and may be especially helpful for children who do not respond to vitamin B6. It may also lessen the risk of blood clots.

Your metabolic doctor will decide whether your child needs betaine. Unless you are advised otherwise, use only betaine prescribed by your doctor.

### **Vitamin B12**

Some people with homocystinuria have low levels of vitamin B12 in their blood. They may need to have vitamin B12 injections. Ask your doctor whether your child needs extra vitamin B12.

### **Folic Acid**

Some people have low levels of folic acid, a type of B vitamin, in their blood. They may need to take folic acid supplements by mouth. This vitamin can help lower the level of homocystine in the blood. Ask your doctor whether your child needs folic acid supplements.

### **L-cystine**

People with homocystinuria may have low levels of another amino acid called L-cystine. L-cystine may already be part of the special medical formula. If not, it can be taken by mouth as a supplement. Unless you are advised otherwise, use only L-cystine prescribed by your doctor.

Do not use any supplements or medications without checking with your metabolic doctor.

### **4. Blood and urine tests**

Your child will have regular blood and urine tests to check his or her amino acid levels. Your child's diet or formula may need to be adjusted based on blood test results.

### **5. Pregnancy**

Pregnancy increases the risk for blood clots, stroke, and heart disease in women with homocystinuria. Women are often given blood thinning medication during the last few months of pregnancy until about 6 weeks after delivery.

The usual treatments for homocystinuria should be continued during pregnancy. In addition to blood clots, untreated women are at higher risk for miscarriage and stillbirth.

## **What happens when homocystinuria is treated?**

With lifelong treatment, many children have normal growth and intelligence. Treatment may lower the chance for blood clots, heart disease, and stroke. Treatment also lessens the chance of eye problems. However, even when treated, some people still develop lens dislocation. This can often be corrected by surgery or other methods.

Children who begin treatment later in life may have mental retardation and behavior problems.

## **What causes the CBS enzyme to be absent or not working correctly?**

Genes tell the body to make various enzymes. People with homocystinuria have a pair of genes that do not work correctly. Because of the changes in this pair of genes, the CBS enzyme either does not work properly or is not made at all.

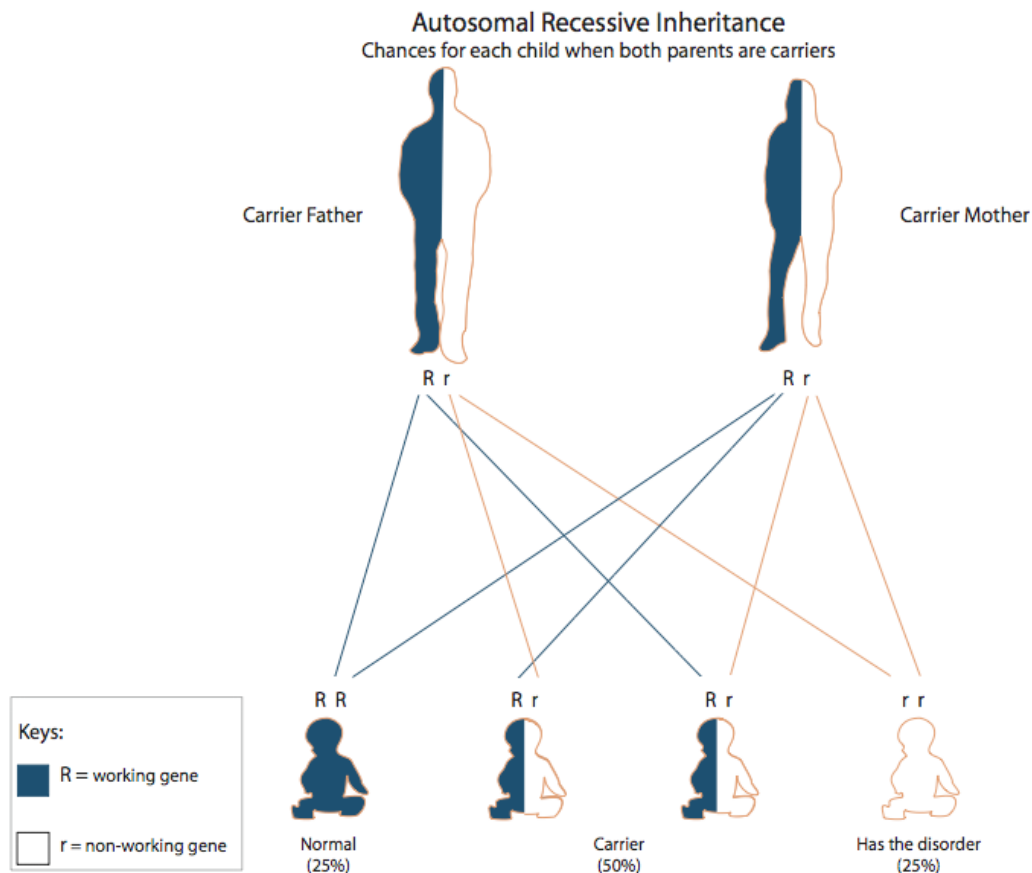
## How is homocystinuria inherited?

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

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

Parents of children with homocystinuria rarely have the condition themselves. Instead, each parent has a single non-working gene for homocystinuria. They are called carriers. Carriers do not have the condition 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 homocystinuria. 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 this condition. Genetic counselors can answer your questions about how it is inherited, options 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 can be done on a blood sample. Genetic testing, also called DNA testing, looks for changes in the pair of genes that cause homocystinuria.

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

## **What other testing is available?**

Homocystinuria is confirmed by special blood and urine tests. People with this condition usually have high levels of homocystine and methionine in their blood. Their urine usually has high levels of homocystine.

The condition can also be confirmed by testing the CBS enzyme in a skin sample.

## **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.

If DNA testing would not be helpful, an enzyme test can be done 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 homocystinuria or be carriers?**

### **Having homocystinuria**

If they are healthy and growing normally, older brothers and sisters of a baby with homocystinuria are unlikely to be affected. However, finding out whether other children in the family have the condition may be important. Early treatment could prevent serious health problems. Ask your metabolic doctor whether your other children should be tested.

### **Homocystinuria carriers**

Brothers and sisters who do not have the condition 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.

Each of the parents' brothers and sisters has 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 chance they are also at risk to have children with homocystinuria.

Some states do not provide newborn screening for homocystinuria. 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 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 can be tested using blood, urine or skin samples.

### **Carrier testing**

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

If DNA testing 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 homocystinuria?**

About one in every 200,000 to one in every 300,000 babies in the United States is born with homocystinuria.

## **Does homocystinuria happen more often in a certain ethnic group?**

This condition occurs in all ethnic groups around the world. It is found more often in white people from the New England region of the United States. It is also more common in people with Irish ancestry. About one in every 50,000 babies in these groups has homocystinuria.

## Does homocystinuria go by any other names?

Homocystinuria is also called:

- Homocystinemia
- Cystathionine beta-synthase deficiency
- CBS deficiency

## Where can I find more information?

National Coalition for PKU and Allied Disorders

<http://www.pku-allieddisorders.org/>

Children Living with Inherited Metabolic Diseases (CLIMB)

<http://www.climb.org.uk>

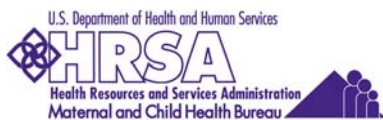
Genetic Alliance

<http://www.geneticalliance.org>

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