



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: Holocarboxylase synthetase deficiency

Also known as: Multiple carboxylase deficiency – neonatal form (MCD)

Acronym: HCSD

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

What is HCSD?

HCSD stands for “holocarboxylase synthetase deficiency”. It is one type of organic acid disorder. People with HCSD have problems changing protein and carbohydrates from food into energy for the body.

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.

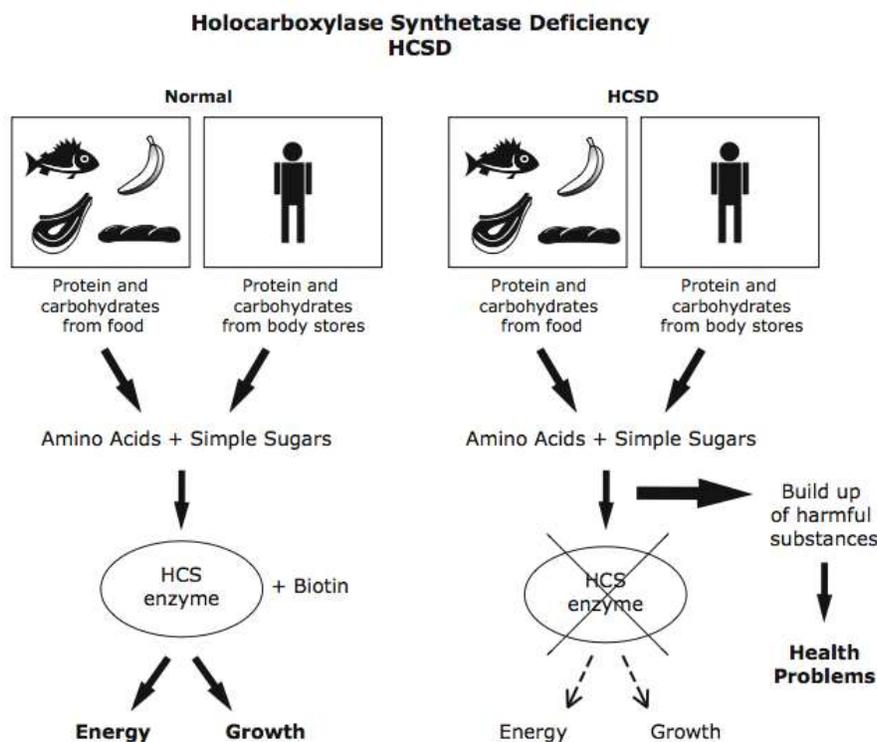
People with organic acid disorders cannot break down protein properly. This causes harmful substances to build up in their blood and urine. These substances can affect health, growth and learning.

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 HCSD?

HCSD occurs when an enzyme called “holocarboxylase synthetase” (HCS), is either missing or not working properly. This enzyme’s job is to add a vitamin called ‘biotin’ to other enzymes called ‘carboxylases’ so that they can change the food we eat into energy for the body. When the HCS enzyme is not working, certain harmful substances build up in the blood and urine. This can cause serious health problems.



If HCSD is not treated, what problems occur?

Each child with HCSD is likely to experience slightly different effects. Many babies with this condition start to have symptoms within hours of birth or during the first few days or weeks of life. Other babies have their first symptoms sometime in infancy, usually before two years of age.

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

HCSD 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
- irritability
- low muscle tone (floppy muscles and joints)
- severe peeling skin rash

Common lab findings are:

- low blood sugar, called hypoglycemia
- high levels of acidic substances in the blood, called metabolic acidosis
- slightly high levels of ammonia in the blood
- low platelets
- ketones in the urine
- high levels of substances called organic acids in the urine

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

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

Untreated children with HCSD often have other symptoms, whether or not they have metabolic crises. These can include:

- skin rashes or skin infections
- hair loss
- learning disabilities or intellectual disabilities
- delays in walking and motor skills
- problems coordinating movements, called ataxia
- rigid muscle tone, called spasticity
- poor growth
- seizures
- hearing loss
- vision loss

Without treatment, most babies with HCSD will die.

What is the treatment for HCSD?

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

The main treatment for HCSD is a type of B vitamin called biotin. In babies found to have HCSD through newborn screening, biotin treatment can prevent symptoms from occurring. It can also reverse some of the health problems in children who have already shown symptoms. You will need a prescription from your doctor in order to purchase the amount of biotin your child will need.

Prompt treatment with biotin is needed to prevent intellectual disabilities and serious medical problems. You should start the treatment as soon as you know your child has HCSD. Your child will need to take biotin by mouth on a daily basis throughout life.

Biotin is usually the only medication needed to treat HCSD. Your child will not need to restrict any activities or change his or her diet.

What happens when HCSD is treated?

Babies who receive prompt and ongoing treatment with biotin before they have a metabolic crisis are expected to have normal growth and development.

Even with treatment, a few children have developed life-long learning problems or intellectual disabilities. In children who have already shown delays in learning, or loss of hearing or eyesight, treatment can prevent additional effects. But, it may not be able to correct the effects that are already present.

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

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

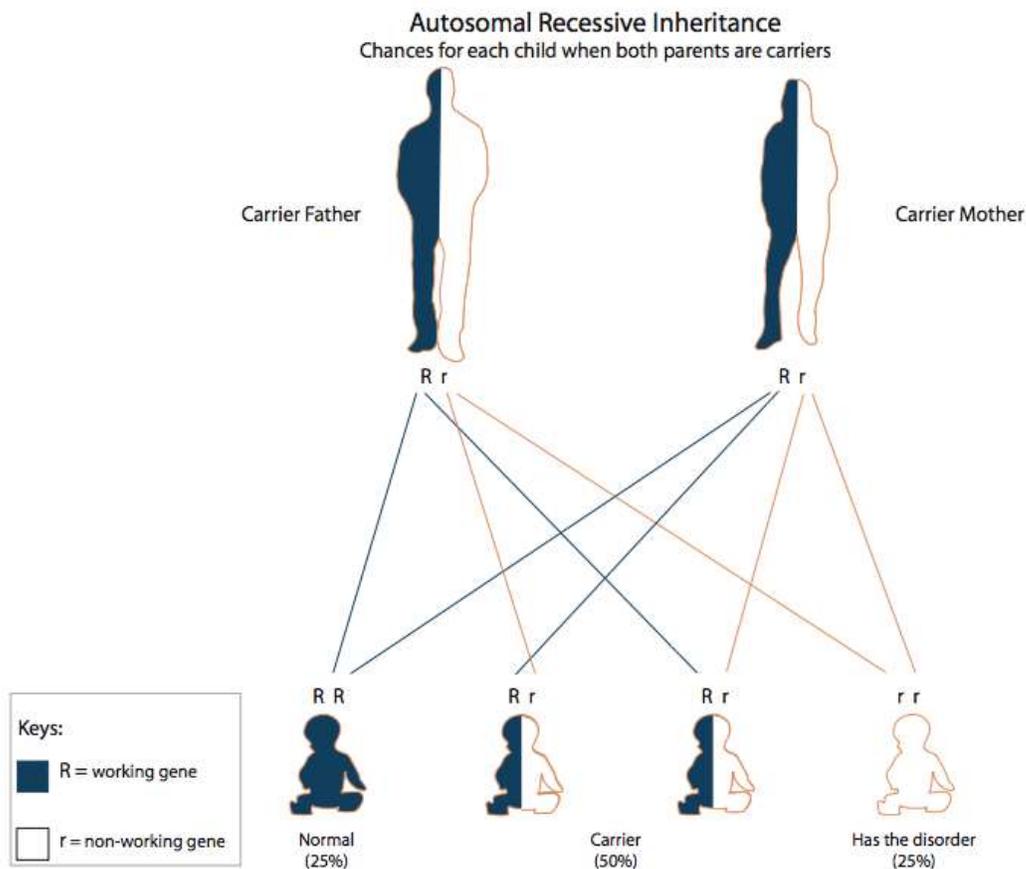
How is HCSD inherited?

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

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

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

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

What other testing is available?

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

Can you test during pregnancy?

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

Having HCSO

Older brothers and sisters of a baby with HCSO 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.

HCSO carriers

Brothers and sister who do not have HCSO 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 an HCSO 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 HCSO.

All states offer newborn screening for HCSD. However, when both parents are HCSD 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

Diagnostic testing on blood or skin samples can be done for brothers or sisters of a child with HCSD. Talk to your doctor or genetic counselor if you have questions about testing for HCSD.

Carrier testing

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

How many people have HCSD?

Less than one in 100,000 babies in the United States is born with HCSD.

Does HCSD happen more frequently in a certain ethnic group?

No, HCSD does not happen more often in any specific race, ethnic group, geographical area, or country.

Does HCSD go by any other names?

HCSD is sometimes also called:

- Holocarboxylase deficiency
- HLCS deficiency
- Multiple carboxylase deficiency, early-onset
- Infant multiple carboxylase deficiency
- MCD, neonatal form
- Early onset combined carboxylase deficiency

Where can I find more information?

Organic Acidemia Association

<http://www.oaaneews.org>

CLIMB (Children Living with Inherited Metabolic Disorders)

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

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

Baby's First Test
<http://www.babysfirsttest.org>

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