



HMG Lyase Deficiency (3-Hydroxy-3-Methylglutaryl-Coa Lyase Deficiency)

What is it?

HMG lyase deficiency is one type of organic acid disorder. People with this condition have problems breaking down an amino acid called leucine from the food they eat.

What causes it?

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.

In order for the body to use fat for energy, enzymes break down fatty acids into ketone bodies. Normally, during long periods without eating, ketones are made by the body and used for fuel.

HMG lyase deficiency occurs when an enzyme, called HMG CoA lyase, is either missing or not working properly. This enzyme has two jobs. The first is to help break down leucine. Leucine is found in all foods that contain protein. The second job is to help the body make ketone bodies from stored fat.

When children with this condition eat food containing leucine, harmful substances build up in the blood. In addition, children with HMG lyase deficiency can't make ketone bodies from stored fat like most people. So, when they don't eat for a long period of time, they can develop low blood sugar (hypoglycemia) and serious health problems.

If HMG lyase deficiency is not treated, what problems occur?

Each child with HMG lyase deficiency will have somewhat different effects. Babies with this condition are usually healthy at birth. Most babies start to have symptoms between 3 months and 2 years of age. A few babies, though, have had their first symptoms just a few days after birth.

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

- 1) Poor appetite.
- 2) Extreme sleepiness or lack of energy.
- 3) Behavior changes.
- 4) Irritable mood.
- 5) Muscle weakness.

Other symptoms then follow:

- 1) Fever
- 2) Nausea
- 3) Diarrhea
- 4) Vomiting
- 5) Hypoglycemia (low blood sugar)
- 6) Increased levels of acidic substances in the blood, called metabolic acidosis
- 7) High levels of ammonia in the blood
- 8) Enlarged liver

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

- 1) Breathing problems.
- 2) Seizures.
- 3) Coma, sometimes leading to death.

If not treated, many babies with HCSLD die.

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

- 1) Skin rashes or skin infections.
- 2) Hair loss.
- 3) Learning disabilities or mental retardation.
- 4) Delays in walking and motor skills.
- 5) Problems coordinating movements, called ataxia.
- 6) Rigid muscle tone, called spasticity.
- 7) Poor growth.
- 8) Seizures.
- 9) Hearing loss.
- 10) Vision loss.

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 mental retardation 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 lifelong learning problems or mental retardation. 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.

Is HCSD inherited?

HCSD is inherited and 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 nonworking 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 percent chance in each pregnancy for the child to have HCSD. There is a 50 percent chance for the child to be a carrier, just like the parents. And, there is a 25 percent chance for the child to have two working genes.

Can other members of the family have HCSD or be carriers?

Having HCSD

The brothers and sisters of a baby with HCSD 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 with your metabolic doctor or genetic counselor about testing your other children.

HCS D Carriers

Brothers and sisters who do not have HCS D still have a chance to be carriers like their parents. Except in special cases, carrier testing should be done only in people over 18.

Each of the parents' brothers and sisters has a 50 percent chance to be an HCS D 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 HCS D.

When both parents are HCS D 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 HCS D. Talk to your doctor or genetic counselor if you have questions about testing for HCS D.

Carrier Testing

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

How many people have HCS D?

About one in 87,000 babies in the United States is born with HCS D.

Does HCS D happen more frequently in a certain ethnic group?

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

Does HCS D go by any other names?

HCS D is sometimes also called:

- 1) Holocarboxylase deficiency.
- 2) HLCS deficiency.
- 3) Multiple carboxylase deficiency, early onset.
- 4) Infant multiple carboxylase deficiency.
- 5) MCD, neonatal form.

Where can I find more information?

Organic Acidemia Association

www.oaaneews.org

Children Living with Inherited Metabolic Diseases (CLIMB)

www.climb.org.uk

Save Babies Through Screening Foundation

www.savebabies.org

Genetic Alliance

www.geneticalliance.org

Children's Special Health Services (CSHS)

State Capitol Judicial Wing

600 E. Boulevard Ave., Department 301

Bismarck, ND 58505-0269

Toll Free: 800.755.2714

701.328.2436

Relay TDD: 701.328.3975

CSHS website: www.ndhealth.gov/CSHS

North Dakota Department of Health website:

www.ndhealth.gov

Family support resources available from CSHS:

- Guidelines of Care Info
- Family Support Packet
- Financial Help Packet
- Insurance Fact Sheet

Family Resources

Family to Family Network
Center for Rural Health
University of North Dakota
School of Medicine and Health Sciences
P.O. Box 9037
Grand Forks, ND 58202-9037
Toll Free: 888.434.7436
701.777.2359
Fax: 701.777.2353
E-mail: NDF2F@medicine.nodak.edu
www.medicine.nodak.edu/crh

Pathfinder Services of ND
Pathfinder Family Center
1600 2nd Ave. SW, Ste. 19
Minot, ND 58701
Toll Free: 800.245.5840
701.837.7500
Relay TDD: 701.837.7501
E-mail: ndpath01@ndak.net
www.pathfinder.minot.com

Family Voices of North Dakota, Inc.
P.O. Box 163
Edgeley, ND 58433
Toll Free: 888.522.9654
701.493.2634
Fax: 701.493.2635
www.geocities.com/ndfy

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

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