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# Multiple Carboxylase Deficiency (MCD) – Organic Acid Disorders

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## What are organic acid disorders?

Organic acid disorders (also sometimes called organic acidemias) are a class of inherited metabolic disorders that occur when the body cannot break certain components of proteins (for example, branched-chain amino acids) and other substances. This leads to an accumulation of harmful substances in the blood and urine, which can cause serious health problems.

## What is Multiple Carboxylase Deficiency?

Carboxylases are important in the production of certain fats and carbohydrates and for the breakdown of proteins. People who have Multiple Carboxylase Deficiency (MCD) have a deficiency in an enzyme called holocarboxylase synthetase. Biotin is a vitamin that is important as a cofactor to activate carboxylase enzymes. Holocarboxylase synthetase adds the biotin to the carboxylases. When holocarboxylase synthetase is deficient, this affects the activity of multiple carboxylases.

## What is its incidence?

Multiple Carboxylase Deficiency is a rare disease that affects about 1 in every 90,000 babies born in Ontario.

## What causes the disease?

Mutations in the gene for holocarboxylase synthetase produce deficient or defective enzymes.

## What are the clinical features of the disease?

Although babies with MCD are normal at birth, without treatment they may have an episode of metabolic crisis with encephalopathy, which can progress to coma and death. The first episode can occur within the first few days of life. Other symptoms include lethargy, poor appetite and failure to thrive, vomiting, low muscle tone, and skin rash.

Increased amounts of acidic substances and ammonia may be found in the blood (acidemia and hyperammonemia). Without treatment, children with MCD can die or develop many different problems, including mental retardation, poor balance and poor coordination, hair and skin problems, seizures, hearing loss, and vision loss. The presentation of MCD is variable and there may be individuals with the disorder who are mildly affected or are asymptomatic.

## How is the diagnosis confirmed?

The diagnosis of MCD is confirmed if a specific urine organic acid profile is found. Enzyme studies and mutation analysis of the gene for holocarboxylase synthetase enzyme may also assist in confirming the diagnosis. Diagnostic testing is arranged by specialists at your regional treatment centre.

## What is the treatment of the disease?

Dietary supplementation with large doses of biotin can prevent symptoms of multiple carboxylase deficiency. This treatment is usually life-long. For symptomatic children, supplementation can reverse some symptoms, such as the biochemical imbalance(s), hair loss, seizures, low muscle tone, and skin rash. Although treatment can halt the progression of developmental delay, hearing loss, and visual impairments, it cannot reverse damage that has already occurred. Treatment is coordinated by specialists at your regional treatment centre.

## What is the outcome of treatment?

If treatment is able to prevent episodes of metabolic crisis, children with MCD have a good prognosis. However, response to treatment and therefore the outcome is variable. Some children who have been treated could still develop a mental handicap or learning problems.

## Can a family have more than one child with MCD?

MCD is inherited as an autosomal recessive disorder. The parents of a child who has MCD are assumed to be carriers for the disorder and have a 1 in 4 (25%) chance, in each pregnancy, of having another child with the disorder. Prenatal testing for MCD can be done as early as 10-12 weeks of pregnancy. Genetic counselling to discuss the benefits of prenatal testing options in more detail is recommended.

Unaffected siblings of a child with MCD have a 2/3 chance of being carriers. Carriers are healthy and do not have symptoms of MCD.

### Resources

<http://www.newbornscreening.info/Parents/organicaciddisorders/HCSO.html>

[http://www.orpha.net//consor/cgi-bin/OC\\_Exp.php?Lng=GB&Expert=148](http://www.orpha.net//consor/cgi-bin/OC_Exp.php?Lng=GB&Expert=148)

<http://www.geneclinics.org/>