
Methylmalonic Acidemia (MUT, Cbl) – Organic Acid Disorders

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 MMA? What causes the disease?

People with methylmalonic acidemia (MMA) cannot process a substance called methylmalonyl-CoA properly, leading to elevated levels of methylmalonic acid in their blood. This can be due to a defect in an enzyme called methylmalonyl-CoA mutase (MUT) or if there is a deficiency or a problem with processing vitamin B12 (the cobalamin defects, Cbl), which is a cofactor of this enzyme.

What is its incidence?

Methylmalonic acidemia is estimated to affect about 1 in every 50,000 babies born in Ontario.

What are the clinical features of the disease?

Although babies with methylmalonic acidemia are normal at birth, without treatment they may have an episode of metabolic acidosis with encephalopathy, which can progress to coma and death. Other symptoms include lethargy, failure to thrive, vomiting, hypotonia, and seizures. Increased amounts of ammonia and acidic substances may be found in the blood (hyperammonemia and acidemia). The presentation of MMA is variable and there may be individuals with the disorder who are mildly affected or are asymptomatic, but may still be at risk for an acute metabolic crisis.

How is the diagnosis confirmed?

The diagnosis of MMA is confirmed by looking for certain substances in the blood and urine. A specific urine organic acid profile, and specific acylcarnitine and amino acid profiles in the blood are helpful in confirming the diagnosis. Enzyme studies and mutation analysis of the genes involved in the metabolism of methylmalonyl CoA 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?

A low protein diet and vitamin B12 injection are often recommended in children with MMA. They should also avoid going long periods without food. Supplementation with carnitine and antibiotics may also be considered. Treatment can prevent metabolic crises and their sequelae. In an acute symptomatic episode, IV glucose and fluids can be given, along with other medications that can help the body to get rid of harmful substances and to decrease the level of acid in the blood. 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 methylmalonic acidemia have a good prognosis. However, response to treatment and therefore the outcome is variable. Even with treatment, some children may still have developmental delays.

Can a family have more than one child with MMA?

MMA is inherited as an autosomal recessive disorder.

The parents of a child who has MMA 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 MMA 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 MMA have a 2/3 chance of being carriers. Carriers are healthy and do not have symptoms of MMA.

Resources

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

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

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