

3-Hydroxy-3-Methylglutaryl-CoA Lyase (HMG) Deficiency (metabolic condition: organic acid disorder)

Also known as:

- HMG-CoA lyase deficiency
- deficiency of hydroxymethylglutaryl-CoA lyase
- hydroxymethylglutaric aciduria

What are organic acid disorders?

Organic acid disorders (sometimes called organic acidemias) are a group of inherited metabolic conditions in which certain components of proteins, for example amino acids, cannot be broken down. This leads to an accumulation of toxic metabolites in the body which can cause serious health problems.

What is HMG deficiency?

3-hydroxy-3-methylglutaryl-CoA lyase (HMG CoA lyase) is an enzyme involved in the breakdown of the amino acid leucine, a component of all proteins. This enzyme is also important in the production of ketones, an energy source for the body. When this enzyme is missing, toxic metabolites accumulate and there is a deficiency of ketones.

What causes HMG deficiency?

HMG deficiency is caused by mutations in the gene for HMG-CoA lyase resulting in absent or decreased enzyme activity.

How common is HMG deficiency?

HMG deficiency is a rare condition reported in fewer than 100 individuals worldwide.

What are the clinical features of HMG deficiency?

HMG deficiency usually presents in the first few weeks of life, but can occur later. Infants with HMG deficiency may develop a metabolic crisis during a minor illness or during a period of fasting. In newborns, the stress of birth may trigger the presentation. Clinical features include lethargy, vomiting, hypotonia and enlarged liver with hypoglycemia, acidosis and hypoketosis. Coma and death may occur if treatment is not started quickly.

What is the screening test for HMG deficiency?

A specific pattern of organic acid metabolites is detected on the newborn blood spot screen. Newborn blood spot screening is not 100% perfect. Infants with clinical symptoms need timely assessment and diagnostic testing even if their screen result is normal.

How is the diagnosis confirmed?

The diagnosis of HMG deficiency is confirmed by detecting specific metabolites in urine or on blood acylcarnitine analysis. Further testing may include enzyme analysis and/or mutation analysis. Specialists at the clinics listed below will arrange diagnostic testing.

How is HMG deficiency treated?

HMG deficiency is treated by avoidance of fasting and dietary supplementation with carnitine. A low protein and low fat diet is usually required. Parent education is an important component of treatment, including advising parents on actions to be taken when their child develops a minor illness. Prompt treatment of a metabolic crisis with intravenous fluids and glucose is necessary. The treatment is lifelong.

What is the outcome of treatment for HMG deficiency?

Prevention and prompt treatment of metabolic crises improves the outcome of HMG deficiency. Even with treatment some patients may develop neurological problems.

Is HMG deficiency inherited?

HMG deficiency is inherited as an autosomal recessive trait. Parents of a child with HMG deficiency are carriers of the condition and have a 1 in 4 chance of having another affected child in each subsequent pregnancy. HMG deficiency carriers are healthy. Genetic counselling and prenatal testing is available to all families with HMG deficiency.

For additional resources, please call:

Clinical & Metabolic Genetics Program (Edmonton)

8-53 Medical Sciences Building
8440 – 112 St. NW
Edmonton, AB T6G 2H7
Phone: 780-407-7333
Fax: 780-407-6845

Emergency consultations:

Phone 780-407-8822 and ask for the specialist on call for metabolic diseases.

Clinical & Metabolic Genetics Program (Calgary)

Alberta Children's Hospital
28 Oki Drive NW
Calgary, AB T3B 6A8
Phone: 403-955-7587
Fax: 403-955-3091

Emergency consultations:

Phone 403-955-7211 and ask for the specialist on call for metabolic diseases.

Early screening, detection and treatment – every infant, every time

For more information about the NMS Program, visit www.ahs.ca/newbornscreening
MARCH 2019 NMS Program Conditions HMG V3

