Alberta Health Services
Alberta Newborn Screening

Talking with Parents > When talking to a parent whose baby has received an abnormal screen result, let them know that an abnormal screen result doesn't mean that the infant has the condition. It means that they have a higher chance of having the condition, and they need more tests to find out for sure. A printable sheet for parents with more condition specific information can be used to support your conversation, visit ahs.ca/nms and under Quick Reference click on *What conditions are screened for?*

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

(metabolic condition: organic acid disorder)

Information for Health Professionals

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 pathogenic variants 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 infants, 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 will not detect all infants with HMG deficiency. 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 molecular genetic analysis. The Clinical and Metabolic Genetics Program 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. Prompt treatment of a metabolic crisis with intravenous fluids and glucose is necessary. Treatment improves the outcome of HMG deficiency. However, some patient may develop neurological problems even with treatment. The treatment is lifelong.

Is HMG deficiency inherited?

HMG deficiency is inherited as an autosomal recessive disorder. 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 is available to families with HMG deficiency.

Additional resources are available through:

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 and follow-up care – every baby, every time

For more information about the Alberta Newborn Screening Program, visit www.ahs.ca/newbornscreening