3-Hydroxy-Isovaleryl Disorders - (3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (HMG), 3-Methylcrotonyl-CoA Carboxylase Deficiency (3MCC), Beta Ketothiolase Deficiency (BKT), and Multiple Carboxylyse Deficiency (MCD))

Organic acid disorders

What is it?

These are a group of inherited organic acid disorders comprised of 3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency (also known as HMG), 3-Methylcrotonyl-CoA Carboxylase Deficiency (also known as 3MCC), Beta Ketothiolase Deficiency (also known as BKT), and Multiple Carboxylyse Deficiency (also known as MCD). People with these organic acid disorders cannot properly break down certain components of protein and sometimes fats (as in HMG). This is because the body is lacking a specific chemical called an enzyme. Since the body cannot properly break down protein, certain organic acids build up in the blood and urine and cause problems when a person eats normal amounts of protein, or becomes sick.

What are the symptoms?

A person with one of these disorders can appear normal at birth. People with these disorders need to receive follow-up care by a team of professionals that is experienced in treating people with metabolic disorders.

The symptoms of HMG can be very variable between people. People may present with vomiting, low blood sugar, low muscle tone, and large livers. Some people with HMG may have no symptoms at all. Many symptoms of HMG can be prevented by immediate treatment and lifelong management.

The symptoms of 3-MCC can be very variable between people. Newborns may present with vomiting, diarrhea, failure to thrive, and seizures. Some people with 3-MCC may have low blood sugar and liver problems while others may have no symptoms at all. Many symptoms of 3-MCC can be prevented by immediate treatment and lifelong management.

The symptoms of BKT include intermittent episodes of severe metabolic acidosis and ketosis accompanied by vomiting, diarrhea and coma that may progress to death. Death or neurological complications can occur. Other symptoms include cardiomyopathy, poor weight gain, renal failure and short stature.

The symptoms of MCD include food refusal, vomiting, skin rashes, breathing problems, hypotonia, seizures and lethargy. Severe metabolic/lactic acidosis, organic aciduria, mild hyperammonemia and variable hypoglycemia can lead to coma and death if not treated.

Inheritance and frequency

These disorders are inherited in an autosomal recessive manner. This means that for a person to be affected with HMG, 3-MCC, BKT or MCD he or she must have inherited two non-working copies of the gene responsible for causing HMG, 3-MCC, BKT or MCD. Usually, both parents of a person affected with an autosomal recessive disorder are unaffected because they are

carriers. This means that they have one working copy of the gene, and one non-working copy of the gene. When both parents are carriers, there is a 1 in 4 (or 25%) chance that both parents will pass on the non working copies of their gene, causing the baby to have either HMG, 3-MCC, BKT or MCD. Typically, there is no family history of HMG, 3-MCC, BKT or MCD in an affected person. HMG is a rare organic acid disorder; the number of people with HMG is not known. It is more common in people from Saudi Arabia. About 1 in 50,000 babies born have 3-MCC. The mother may also be tested as well because several cases of maternal 3-MCC deficiency have been identified following an abnormal newborn screening result in their off spring. About 1 in 87,000 babies born have MCD. BKT is a rare organic acid disorder; the frequency of BKT in the general population is unknown.

How is it detected?
These disorders may be detected through newborn screening. A recognizable pattern of elevated chemicals alerts the laboratory that a baby may be affected. Confirmation of newborn screening results is required to make a firm diagnosis. This is usually done by a physician that specializes in metabolic conditions, or a primary care physician.

How is it treated?
These disorders may be treated with a special diet that is low in protein and sometimes fat. A special medication may also be recommended. A special medication may also be recommended. A specifically tailored treatment regimen is typically provided by a metabolic genetics professional.

DISCLAIMER: This information is not intended to replace the advice of a genetic metabolic medical professional.

For more information:

Genetics Home Reference
Website: http://www.ghr.nlm.nih.gov

Save Babies Through Screening Foundation
4 Manor View Circle
Malvern, PA 19355-1622
Toll Free Phone: 1-888-454-3383
Fax: (610) 993-0545
Email: email@savebabies.org
Website: http://www.savebabies.org

Organic Acidemia Association
13210 - 35th Avenue North
Plymouth, MN 55441
Phone: 763-559-1797
Fax: 763-694-0017
Email: oaanews@aol.com
www.oaanews.org

American College of Medical Genetics
Newborn Screening ACT Sheets and Confirmatory Algorithms
http://www.acmg.net/resources/policies/ACT/condition-analyte-links.htm

Cardinal Glennon Children's Hospital
St. Louis, Missouri
314-577-5639
Website: http://pediatrics.slu.edu/index.phtml?page=geneticsdiv

Children's Hospital at University Hospital and Clinics
Columbia, Missouri
573-882-6991
Website: http://www.genetics.missouri.edu/

Children's Mercy Hospital
Kansas City, Missouri
816-234-3290
Website: http://www.childrens-mercy.org/content/view.aspx?id=155

St. Louis Children's Hospital
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314-454-6093
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