

Disease Name:

3-METHYLGLUTACONIC ACIDURIA TYPE I
(3-METHYLGLUTACONYL-CoA HYDRATASE DEFICIENCY; 3-MG-CoA-HYDRATASE DEFICIENCY; MGA, TYPE I)

Classification: Organic aciduria

Genetic Information:

Inheritance: Organic aciduria

Population Incidence: Rare, less than 20 cases described

Ethnic Incidence: No known population at increased risk

Gene & Location: Type I- gene AUH on 9q22.2

Common Mutation: No known common mutations

OMIM # #250950; *600529

Disease Information:

Symptom Onset: Variable, from infancy to early childhood

Symptoms: Symptoms range from minimal to severe. Two different phenotypes have been identified. Mildly affected individuals have had speech retardation, short attention span and methylglutaconic aciduria (MGA) as the only features. Severely affected individuals, in addition to MGA, have presented with acidosis, hypotonia; hepatomegaly; microcephaly; macrocephaly; spastic quadriplegia; dystonia, atrophy of the basal ganglia; insomnia; irritability; self-mutilation; crying fits; dementia; enuresis; developmental delay; coma and gastroesophageal reflux disease. Fasting has produced hypoglycemia and acidosis in some patients. The neurological changes on MRI have been progressive in some patients even when clinically stable and on therapy. MGA has been identified in asymptomatic infants, children and adults and may be also be present in a number of acute medical conditions such as urea cycle defects, hypercholesterolemia, mitochondrial disease and pregnancy.

Physical Findings: No dysmorphisms, the neurological findings are variable.

Treatment: Carnitine supplementation and modest leucine restriction may be beneficial for these children, especially if diagnosed presymptomatically.

Natural History without treatment: Variable with asymptomatic patients to patients with severe neurological dysfunction with possible hypoglycemia and acidosis with fasting.

Natural History with treatment: Theoretically will have improved neurological status and fewer problems with fasting or illness. However, this has not been proven

Metabolic Information: **Missing Enzyme & Location:** 3-methylglutaconyl-CoA hydratase- presumably located in the mitochondria of all tissues

MS/MS profile: C5-OH (3-hydroxyisovaleryl carnitine) - elevated

Prenatal testing: Possible with enzyme assay of amniocytes or CVS

Miscellaneous Information:

Prepared for the NW Regional Newborn Screening Program by Sara Copeland MD, Judith Tuerck RN MS and Lorinda Paradise at OHSU in Portland, OR.

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