

Disease Name:

**2-METHYL-3-HYDROXYBUTYRYL-CoA
DEHYDROGENASE DEFICIENCY**
(HYDROXYL-CoA DEHYDROGENASE DEFICIENCY; 3-HYDROXY-2-
METHYLBUTYRYL-COA DEHYDROGENASE DEFICIENCY)

Classification: Organic aciduria

**Genetic
Information:**

Inheritance: X-linked; but an affected female has been identified

Population Incidence: Rare, less than 10 reported cases

Ethnic Incidence: No known population at increased risk

Gene & Location: Xp11.2- AMYLOID BETA-BINDING POLYPEPTIDE; ERAB
2-METHYL-3-HYDROXYBUTYRYL-CoA DEHYDROGENASE; MHBD

Common Mutation: No known common mutations

OMIM # #300438; *300256

**Disease
Information:**

Symptom Onset: As neonates and children, usually after a stressor such as illness or vaccinations

Symptoms: The majority of cases have an early asymptomatic period from 9-14 months followed by progressive and usually severe loss of motor skills, choreoathetosis, dystonia and seizures. Sensory deficits in some patients have included retinal degeneration and hearing loss. One patient presented in the newborn period with hyperammonemia, hypoglycemia and acidosis if metabolic decompensation. Mild cerebral white matter changes on MRI with spastic diplegia have been noted. A mild case was apparently normal until age 6 before deterioration was noted after a viral infection.

Physical Findings: Progressive loss of skills and neurological impairment. Mental retardation with epilepsy. No particular dysmorphisms.

Treatment: Isoleucine and protein restriction has resulted in some improvement of biochemical parameters and physical symptoms. In two cases no further neurological deterioration occurred, but lost function was not regained.

Natural History without treatment: Uncertain, as all diagnosed patients have been treated, whether neurological deterioration would progress to death. The oldest patient (also the mildest) is severely disarthric and works in a sheltered workshop.

Natural History with treatment: Uncertain what long-term therapy will show, but seemed to be some clinical improvement with dietary isoleucine restriction.

Metabolic Information:

Missing Enzyme & Location: 2-METHYL-3-HYDROXYBUTYRYL-CoA DEHYDROGENASE- Defect is in the mitochondrial oxidation of 2-methyl branched-chain fatty acids and isoleucine

MS/MS profile: C5-OH methylcrotonyl carnitine- elevated
C5:1 carnitine- elevated
Isoleucine- elevated

Prenatal testing: Theoretically can do prenatal testing on amniocytes or CVS cells for enzyme assay

Miscellaneous Information:

Prepared for the NW Regional Newborn Screening Program

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