

Disease Name:

ISOVALERIC ACIDEMIA/ACIDURIA
(ISOVALERIC ACID CoA DEHYDROGENASE DEFICIENCY; IVA; IVD)

Classification: Organic Acid Disorder

Genetic Information:

Inheritance: Autosomal recessive

Population Incidence: Uncertain, 1/230,000

Ethnic Incidence: No known population at increased risk

Gene & Location: 15q14-q15- IVD gene

Common Mutation: At least 5 different classes of mutations have been identified

OMIM # #243500

Disease Information:

Symptom Onset: Usually within the first 14 days of life in the acute form and later in the chronic form.

Symptoms: Infants with the **acute neonatal** form present after a few days of normalcy with poor feeding, vomiting, severe metabolic keto-acidosis, progressing to coma and death. Dehydration, hyperammonemia, hypocalcemia, hepatomegaly and hyper/hypoglycemia are often present. Depressed bone marrow function with neutropenia, thrombocytopenia and pancytopenia can lead to infection and/or cerebral hemorrhage. Most, but not all, will have the characteristic odor of “sweaty socks” which comes from the accumulation of isovaleryl acids.

The **chronic intermittent** form presents later in infancy or childhood with episodes of metabolic acidosis as described above, usually associated with an intercurrent illness or increased protein load. Pancreatitis has occurred in a number of patients. The different forms can occur in the same family, so are not related to genotype.

Physical Findings: No particular dysmorphisms.

Treatment: Avoidance of fasting, low-protein diet with restricted leucine intake, in combination with glycine and carnitine supplements. Glycine and carnitine allow for the nontoxic removal of excess isovaleric-CoA. Patients will often self-select a low protein diet.

Natural History without treatment: About 50% of patients with the acute neonatal form will die in their first episode. Survivors may have neurological damage, although several patients have had complete neurological recovery. Patients with the chronic form may have neurological damage, but most have normal growth and development. Death from acidotic episodes can occur at any age.

Natural History with treatment: Intellectual prognosis depends on early diagnosis and treatment and subsequently on long-term compliance. If treated appropriately most will have normal development.

Metabolic Information:

Missing Enzyme & Location: Isovaleryl-CoA dehydrogenase is the first step in branched chain organic acid metabolism of leucine.

MS/MS profile: C5 (isovaleryl/ 2-methylbutyryl carnitine)- elevated

Prenatal testing: Prenatal diagnosis is possible via assay of isovalerylglycine in the amniotic fluid and/or by enzyme assay of chorionic villi.

Miscellaneous Information:

Need to differentiate from 2-methylbutyryl dehydrogenase deficiency.

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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