



Isovaleric Acidemia Information for Health Professionals

Isovaleric acidemia is an organic acid disorder in which individuals cannot metabolize leucine.

✓ Clinical Symptoms

Symptoms of isovaleric acidemia can begin shortly after birth through childhood. Isovaleric acidemia causes periods of metabolic crisis. Early symptoms of a crisis include: feeding difficulty, lethargy, hypothermia, and a “sweaty feet” odor. If untreated, symptoms include: metabolic acidosis, ketonuria, thrombocytopenia, neutropenia, hyperammonemia, seizures, cerebral hemorrhage, coma, and death. Survivors of repeated metabolic crisis can have brain damage. In individuals who do not show symptoms until childhood, metabolic crisis can be triggered by illness, infection, or high protein intake.

Some children still have metabolic crises, even when treated, though crises occur less frequently as the child ages.

✓ Incidence

Isovaleric acidemia occurs in less than 1 in 100,000 births.

✓ Genetics of isovaleric acidemia

Mutations in the IVD gene cause isovaleric acidemia. Mutations in this gene reduce or eliminate the activity of the enzyme isovaleryl-CoA dehydrogenase. This enzyme is necessary for breaking down isovaleryl-CoA, which is produced during the metabolism of the amino acid leucine. This causes the accumulation of isovaleric acid in the blood, which causes symptoms of this condition.

✓ How do people inherit isovaleric acidemia?

Isovaleric acidemia is inherited in an autosomal recessive manner. Parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but do not show signs and symptoms of the condition. Each pregnancy between carrier parents has a 25% chance of producing a child affected with isovaleric acidemia, a 50% chance of producing an unaffected carrier child, and a 25% chance of producing a child who is unaffected and is not a carrier.

✓ Treatment

Immediate diagnosis and treatment of isovaleric acidemia is critical to normal development and survival. Individuals should follow a low-leucine, low-protein diet, which generally requires medical foods and formulas. L-carnitine supplementation and glycine may be recommended. Symptoms of a metabolic crisis require immediate medical treatment which may require IV medications, such as bicarbonate and glucose.

✓ **Screening Methodology**

Primary newborn screening for isovaleric acidemia utilizes tandem mass spectrometry to determine the levels of C5 acylcarnitine (isovaleryl/ 2-methylbutyryl carnitine). Elevated levels of C5 indicate the possibility of isovaleric acidemia. False positive and false negative results are possible with this screen.

✓ **What to do After Receiving Presumptive Positive IVA Screening Results**

- 1) **The clinician should immediately check on the clinical status of the baby.**
- 2) **Consultation with a metabolic specialist is essential.**
- 3) **The specialist may request confirmatory lab tests on the baby.**
- 4) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
- 5) **Report Clinical Findings to Newborn Screening Program at 785-291-3363.**
- 6) **Same birth siblings (twins, triplets) of infants diagnosed with isovaleric acidemia should be re-screened; additional testing of these siblings also may be indicated.**

✓ **Confirmation of Diagnosis**

The diagnosis of isovaleric acidemia is confirmed through plasma acylcarnitine analysis revealing elevated C5. Urine organic acid analysis will show isovalerylglycine in most cases of isovaleric acidemia.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive isovaleric acidemia newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with the Kansas Administrative Regulation 28-4-502, it is the responsibility of the attending physician or other birth attendant to obtain repeat specimens when needed to complete the screening process.

If a baby is diagnosed with isovaleric acidemia, the following points should be conveyed to parents:

- ***Parents should understand that treatment for isovaleric acidemia will be life long.***
- ***Parents should understand that treatment is not curative and that all morbidity cannot necessarily be prevented. Long-term management, monitoring, and compliance with treatment recommendations are essential to the child's well-being. A multidisciplinary approach is recommended and should include the following specialties: pediatrics, metabolic disease specialist, and dietician.***
- ***Genetic counseling services may be indicated. A list of counselors and geneticists, whose services are available in Kansas, should be given to the parents if they have not already seen a geneticist.***

For consultation, contact:

Bryce Heese, MD
Biochemical Genetics
Children's Mercy Hospital- Kansas City, MO

Clinic phone: 816-234-3771
Hospital Operator: 816-234-3000
Office Fax: 816-302-9963