



Propionic Acidemia Information for Health Professionals

Propionic acidemia is an organic acid disorder in which individuals are lacking or have reduced activity of the enzyme propionyl-CoA carboxylase, leading to propionic acidemia.

✓ Clinical Symptoms

Symptoms generally begin in the first few days following birth. Metabolic crisis can occur, particularly after fasting, periods of illness/infection, high protein intake, or during periods of stress on the body. Symptoms of a metabolic crisis include lethargy, behavior changes, feeding problems, hypotonia, and vomiting. If untreated, metabolic crises can lead to tachypnea, brain swelling, cardiomyopathy, seizures, coma, basal ganglia stroke, and death. Many babies die within the first year of life. Lab findings during a metabolic crisis commonly include urine ketones, hyperammonemia, metabolic acidosis, low platelets, low white blood cells, and high blood ammonia and glycine levels.

Long term effects may occur despite treatment and include developmental delay, brain damage, dystonia, failure to thrive, short stature, spasticity, pancreatitis, osteoporosis, and skin lesions.

✓ Incidence

Propionic acidemia occurs in greater than 1 in 75,000 live births and is more common in Saudi Arabians and the Inuit population of Greenland.

✓ Genetics of propionic acidemia

Mutations in the PCCA and PCCB genes cause propionic acidemia. Mutations prevent the production of or reduce the activity of propionyl-CoA carboxylase, which converts propionyl-CoA to methylmalonyl-CoA. This causes the body to be unable to correctly process isoleucine, valine, methionine, and threonine, resulting in an accumulation of glycine and propionic acid, which causes the symptoms seen in this condition.

✓ How do people inherit propionic acidemia?

Propionic 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 propionic 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 propionic acidemia in the neonatal period is critical to normal development and survival. Treatment is more effective the earlier it begins. Individuals should follow a low-protein diet which restricts leucine, valine, threonine, and methionine. Medical foods and formulas may be required. Certain medications, such as L-carnitine, antibiotics, and biotin, may be recommended. Regular blood and urine tests are needed to check ketone and amino acid levels. During illness, children may need to be admitted for medical care to prevent a metabolic crisis and fasting should always be avoided.

✓ Screening Methodology

Primary newborn screening for propionic acidemia utilizes tandem mass spectrometry. Elevated levels of C3 indicate the possibility of propionic acidemia. Elevated C3 (propionylcarnitine) is also a marker for methylmalonic acidemia. Additional metabolic studies are needed to distinguish between these two disorders. False positives and false negatives are possible with this screen.

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

- 1) **The clinician should immediately check on the clinical status of the baby.**
- 2) **Consultation with a metabolic specialist is essential.**
- 3) **Urine organic acid analysis and other labs may be recommended.**
- 4) **Call KS Newborn Screening Program at 785-291-3363 with questions about results.**
- 5) **Report clinical findings to the Newborn Screening Program at 785-291-3363.**
- 6) **Same birth siblings (twins, triplets) of infants diagnosed with PROP should be re-screened; additional testing of these siblings also may be indicated.**

✓ **Confirmation of Diagnosis**

The diagnosis of propionic acidemia is confirmed through plasma acylcarnitine analysis revealing increased C3. Urine organic acids should show propionic aciduria. An increase in glycine may be present on blood amino acid analysis.

✓ **Communication of Results to Parents**

If a baby has a presumptive positive propionic acidemia newborn screening result, additional testing needs to be performed to confirm a diagnosis. In accordance with 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 PROP, the following points should be conveyed to parents:

- ***Parents should understand that treatment for propionic acidemia will be lifelong.***
- ***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 pediatrics, metabolic specialists, and dieticians.***
- ***Periodic blood and urine analysis is needed.***
- ***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:

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