

Elevated C3 Acylcarnitine Propionic Acidemia and Methylmalonic Acidemia

Differential Diagnosis: Propionic acidemia (PROP) or (PA); Methylmalonic acidemias (MMA), including defects in B12 synthesis and transport; maternal severe B12 deficiency.

Condition Description: Propionic acidemia (PA); is caused by a defect in propionyl-CoA carboxylase, which converts propionyl-CoA to methylmalonyl-CoA; MMA results from a defect in methylmalonyl-CoA mutase (MUT), which converts methylmalonyl-CoA to succinyl-CoA, or from lack of the required B12 cofactor for methylmalonyl-CoA mutase (cobalamin A, B, C, D, E, F, G, and J).

Conditions associated with this analyte have been identified by the Society of Inherited Metabolic Disorders (SIMD) as critical, and require immediate action.

MEDICAL EMERGENCY: Take the Following IMMEDIATE Action

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Immediate telephone consultation with pediatric metabolic specialist (See attached list).
- Evaluate the newborn; check urine for ketones, and if elevated or infant is ill, initiate emergency treatment as indicated by metabolic specialist and transport immediately to tertiary center with metabolic specialist.
- Initiate timely confirmatory/diagnostic testing as recommended by specialist.
- Initial testing: plasma amino acids, plasma acylcarnitine profile, plasma total homocysteine and urine organic acids.
- Repeat newborn screen if second screen has not been done.
- Educate family about signs, symptoms and need for urgent treatment of hyperammonemia and metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea).
- Report findings to newborn screening program.

Diagnostic Evaluation: Plasma acylcarnitine confirms the increased C3. Blood amino acid analysis may show increased glycine. Urine organic acid analysis will demonstrate increased metabolites characteristic of propionic acidemia or increased methylmalonic acid characteristic of Methylmalonic acidemia. Plasma total homocysteine will be elevated in the cobalamin C, D, E, F, G and J deficiencies. Serum vitamin B12 may be elevated in the cobalamin disorders.

Clinical Considerations: Patients with PA and severe cases of MMA typically present in the neonate with metabolic ketoacidosis, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Long-term complications are common; early treatment may be lifesaving, and continued treatment may be beneficial.

Additional Information:

American College of Medical Genetics and Genomics

<https://www.acmg.net/StaticContent/ACT/C3.pdf>

Genetics Home Reference

PROP <http://ghr.nlm.nih.gov/condition=propionicacidemia>

MMA <http://ghr.nlm.nih.gov/condition=methylmalonicacidemia>

STAR G FELSI

<http://www.newbornscreening.info/Pro/facts.html>

<http://www.newbornscreening.info/Parents/facts.html>