ACMG American College of Medical Genetics and Genomics
Translating Genes Into Health®

ACT Sheet

Newborn Screening ACT Sheet

[Elevated C3 Acylcarnitine]

Propionic Acidemia (PA) and Methylmalonic Acidemia (MMA)

Differential Diagnosis: Propionic acidemia (PA); methylmalonic acidemia (MMA); disorders of vitamin B12 absorption, transport, and processing (cobalamin A, B, C, D, F, J and X, intrinsic factor, transcobalamin II, and transcobalamin receptor deficiencies); maternal vitamin B12 deficiency; succinate-CoA ligase deficiency

Condition Description: PA and MMA are organic acid disorders in which the body is not able metabolize certain proteins and fats. PA is caused by defects in propionyl-CoA carboxylase, leading to elevated propionate metabolites and C3-acylcarnitine. MMA is a heterogenous group of conditions caused by a primary deficiency of methylmalonyl-CoA mutase, or by disruptions in the processing or transport of vitamin B12 (cobalamin A, B, C, D, F, J, or X deficiency; transcobalamin II deficiency, transcobalamin receptor defect, intrinsic factor deficiency), leading to elevated methylmalonate metabolites and of C3. For both PA and MMA, the abnormal accumulation of organic acids can produce severe toxicity within a few days after birth.

You Should Take the Following IMMEDIATE Actions:

- Inform family of the newborn screening result.
- Ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Consult with pediatric metabolic specialist the same day.
- Evaluate the newborn (dehydration, ketonuria, vomiting, hypoglycemia, failure to thrive). If any of these findings are present or the newborn is ill, transport to a hospital for further treatment in consultation with the metabolic specialist.
- Initiate confirmatory/diagnostic testing and management as recommended by the specialist.
- Provide the family with basic information about these disorders and their management, including the need for urgent treatment of hyperammonemia and metabolic acidosis.
- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: Plasma acylcarnitines: C3 is elevated in PA and in all forms of MMA. Urine organic acids: MMA and PA show distinct patterns of methylmalonate or propionate metabolites respectively. Plasma total homocysteine: is elevated in B12-related defects. Plasma methylmalonic acid is elevated in MMAs, but not in PA. Plasma amino acids may show decreased methionine in B12-related conditions. The finding of a low serum B12 level may be secondary to a maternal vitamin B12 deficiency and a maternal B12 level should be ordered. Molecular genetic testing may be required to confirm the diagnosis.

Clinical Considerations: PA and MMA can present acutely in the neonate with lethargy, vomiting, metabolic ketoacidosis, hyperammonemia, and hypoglycemia. Long-term complications are common; early treatment may be lifesaving and long-term treatment is essential. Some forms of MMA are successfully treated with vitamin B12. Succinate-CoA ligase deficiency is a rare neurometabolic disorder.

Additional Information:

How to Communicate Newborn Screening Results
Emergency Protocols (New England Consortium of Metabolic Programs) (PA | MMA)
Gene Reviews (PA | MMA)
Medline Plus (PA | MMA)
Condition Information for Families- HRSA Newborn Screening Clearinghouse (PA | MMA)
ClinGen Actionability Report

Referral (local, state, regional, and national):

Find a Genetics Clinic Directory
Genetic Testing Registry

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State and Other Resources

State Newborn Screening Program

Newborn Screening Program, Utah Department of Health and Human Services
801-584-8256, newbornscreening.health.utah.gov/

Genetics/Metabolic Consultants

Pediatric Medical Genetics, University of Utah Department of Pediatrics
801-213-3599, healthcare.utah.edu/pediatrics/programs-services/genetics.php

Information for Clinicians and Families

Utah Medical Home Portal (see Newborn Disorders and Parents & Families sections)
ut.medicalhomeportal.org/newborn/propionic-acidemia

Parent/Family Support

Organic Acidemia Association
www.oaanews.org/hmg.html

National Resources (with web addresses)

Additional Information

How to Communicate Newborn Screening Results
www.hrsa.gov/sites/default/files/hrsa/advisory-committees/heritable-disorders/resources/achdnc- communication-guide-newborn.pdf

Emergency Protocols (New England Consortium of Metabolic Programs)
www.newenglandconsortium.org/propionic-acidemia

Gene Reviews
www.ncbi.nlm.nih.gov/books/NBK92946/

Medline Plus
medlineplus.gov/genetics/condition/propionic-acidemia/

Condition Information for Families-HRSA Newborn Screening Clearinghouse
newbornscreening.hrsa.gov/conditions/propionic-acidemia

Referral (local, state, regional and national)

Find a Genetics Clinic Directory
clinics.acmg.net

Genetic Testing Registry
www.ncbi.nlm.nih.gov/gtr/