

## 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 to 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 heterogeneous 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](#)

**Local Resources (Insert Local Website Links)**  
**State Resource Site (Insert Website Information)**

<b>Name</b>	
<b>URL</b>	
<b>Comments</b>	

**Local Resource Site (Insert Website Information)**

<b>Name</b>	
<b>URL</b>	
<b>Comments</b>	

**Appendix (Resources with Full URL Addresses)**

**Additional Information**

**How to Communicate Newborn Screening Results**

- <https://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)**

- <https://www.newenglandconsortium.org/propionic-acidemia>
- <https://www.newenglandconsortium.org/methyl>

**Gene Reviews**

- <https://www.ncbi.nlm.nih.gov/books/NBK92946/>
- <https://www.ncbi.nlm.nih.gov/books/NBK1231/>

**Medline Plus**

- <https://medlineplus.gov/genetics/condition/propionic-acidemia/>
- <https://medlineplus.gov/genetics/condition/methylmalonic-acidemia/>

**Condition Information for Families-HRSA Newborn Screening Clearinghouse**

- <https://newbornscreening.hrsa.gov/conditions/propionic-acidemia>
- <https://newbornscreening.hrsa.gov/conditions/methylmalonic-acidemia-methylmalonyl-coa-mutase>

**ClinGen Actionability Report**

- <https://actionability.clinicalgenome.org/ac/Pediatric/ui/stg2SummaryRpt?doc=AC122>

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

**Find a Genetics Clinic Directory**

- <https://clinics.acmg.net>

**Genetic Testing Registry**

- <https://www.ncbi.nlm.nih.gov/gtr/>

This practice resource is designed primarily as an educational resource for medical geneticists and other clinicians to help them provide quality medical services. Adherence to this practice resource is completely voluntary and does not necessarily assure a successful medical outcome. This practice resource should not be considered inclusive of all proper procedures and tests or exclusive of other procedures and tests that are reasonably directed to obtaining the same results. In determining the propriety of any specific procedure or test, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. Clinicians are encouraged to document the reasons for the use of a particular procedure or test, whether or not it is in conformance with this practice resource. Clinicians also are advised to take notice of the date this practice resource was adopted, and to consider other medical and scientific information that becomes available after that date. It also would be prudent to consider whether intellectual property interests may restrict the performance of certain tests and other procedures.