

Newborn Screening ACT Sheet [Elevated C3 Acylcarnitine] Propionic Acidemia and Methylmalonic Acidemia

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

Condition Description: 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** which converts methylmalonyl-CoA to succinyl-CoA or from lack of the required B₁₂ cofactor for methylmalonyl-CoA mutase (cobalamin A, B, C, D, and F).

YOU SHOULD TAKE THE FOLLOWING ACTIONS IMMEDIATELY:

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Consult with pediatric metabolic specialist.
- 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.
- 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 and F 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:

Emergency Protocols (New England Consortium of Metabolic Programs)

[PA](#)
[MMA](#)

Gene Reviews

[PA \(Organic Acidemias Overview\)](#)
[MMA](#)

Genetics Home Reference

[PA](#)
[MMA](#)

Referral (local, state, regional and national):

Testing

[PA](#)
[MMA](#)

[Clinical Services](#)

[Find Genetic Services](#)

Disclaimer: This guideline is designed primarily as an educational resource for clinicians to help them provide quality medical care. It 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. Adherence to this guideline does not necessarily ensure a successful medical outcome. 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 guideline. Clinicians also are advised to take notice of the date this guideline was adopted, and to consider other medical and scientific information that become available after that date.

LOCAL RESOURCES: Insert State newborn screening program web site links

Resource site (insert state newborn screening program website information)

Name	<input type="text"/>
URL	<input type="text"/>
Comments	<input type="text"/>

APPENDIX: Resources with Full URL Addresses

Additional Information:

Emergency Protocols (New England Consortium of Metabolic Programs)

PA

<http://newenglandconsortium.org/for-professionals/acute-illness-protocols/organic-acid-disorders/propionic-acidemia/>

MMA

<http://newenglandconsortium.org/for-professionals/acute-illness-protocols/organic-acid-disorders/methylmalonic-acidemia/>

Gene Reviews

PA (Organic Acidemias Overview)

<http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=NexQvDbtfnPSK&gry=&fcn=y&fw=SoH9&filename=/profiles/oa-overview/index.html>

MMA

<http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=NexQvDbtfnPSK&gry=&fcn=y&fw=QtIb&filename=/profiles/mma/index.html>

Genetics Home Reference

PA

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

MMA

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

Referral (local, state, regional and national):

Testing:

PA

http://www.genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888891&fcn=c&qry=22169&res=nous&res=nointl&key=NexQvDbtfnPSK&show_flag=c

MMA

http://www.genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888891&fcn=c&qry=22174&res=nous&res=nointl&key=NexQvDbtfnPSK&show_flag=c

Clinical Services:

<http://www.ncbi.nlm.nih.gov/sites/genetests/clinic?db=genetests>

Find Genetic Services

<http://www.acmg.net/GIS/Disclaimer.aspx>

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