

Acylcarnitines: Elevated C3 with or without elevated C3/C2 ratio

Possible inborn errors of metabolism

- Propionic Acidemia (PA)
- Methylmalonic Acidemia (MMA)
- Cobalamin (vitamin B12) disorders

Fact Sheet for Providers

What could elevations in C3 with or without elevated C3/C2 ratio indicate?



Elevations in C3 with or without elevated C3/C2 ratio can be indicators of a number of metabolic conditions. Elevations in these analytes indicate a deficiency of certain enzymes involved in amino acid metabolism resulting in the buildup of organic acids in the body. These conditions include PA, MMA, and inborn errors of cobalamin metabolism (e.g., cobalamin C [clbC] deficiency). This result may also be reported if the infant or mother has a vitamin B12 deficiency. Additional testing is needed to determine a specific diagnosis.

Deficiency of the propionyl-CoA carboxylase enzyme causes PA and deficiency of the methylmalonyl CoA mutase enzyme causes MMA. The most common inborn error of cobalamin metabolism is clbC deficiency, also known as methylmalonic aciduria with homocystinuria. CblC deficiency is a rare genetic condition affecting how the body processes vitamin B12, although blood levels of B12 may appear normal.

Early diagnosis and treatment can prevent fatal metabolic crises and other health concerns.

How are these conditions diagnosed?

Infants with a positive newborn screening result should have additional biochemical and molecular testing that may include:

- Plasma quantitative acylcarnitine profile
- Plasma quantitative analysis of amino acids
- Urine organic acids
- Total homocysteine
- Molecular genetic testing

How do I handle an abnormal screening for these conditions?



If one of your patients has a positive newborn screening result, you will be contacted by the Newborn Screening Follow-Up team housed within UNC Pediatric Genetics & Metabolism. Follow-up will likely first include a request for a repeat newborn screening and additional biochemical testing. If results are abnormal, then referral to a pediatric metabolic specialist may be recommended. If there are clinical concerns about the infant, urgent or emergent evaluation may be recommended at the nearest emergency department.

What are the signs and symptoms of PA, MMA, and cobalamin disorders?



Symptoms may not be visible at birth. Common symptoms in the first months of life in those with untreated diagnoses may include the following:

- Poor weight gain or growth
- Weak/low muscle tone
- Vomiting
- Dehydration
- Feeding problems
- Low energy, lethargy
- Pale appearance
- Eye abnormalities (maculopathy/retinal degeneration)
- Seizures
- Metabolic acidosis
- Hyperammonemia
- Megaloblastic anemia

Infants may be critically ill with severe acidosis and/or hyperammonemia before newborn screening results return.

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How are PA, MMA, and cobalamin disorders treated?

After a diagnosis is confirmed, the overall goal of treatment is to prevent the toxic buildup of downstream products to reduce the risk of metabolic acidosis. Primary treatment may include the following:

Treatment	Conditions		
	PA	MMA	Cobalamin Disorders
Lifelong low-protein diet and medical formula	X	X	
Regular and frequent meals and snacks	X	X	
Vitamin B12 supplements		X	X
Carnitine supplementation	X	X	
Antibiotics	X	X	
Folic acid			X
Betaine			X
Medications to prevent hyperammonemia	X		
Buffer to control acidosis	X	X	

Where do I go for more information?

Use your phone's camera to scan the QR codes below.



Resources for PA, MMA, and cobalamin disorders:



[GeneReviews](#)



[MedlinePlus](#)



[ACMG ACT Sheets](#)

Where do I send parents for more information?

Use your phone's camera to scan the QR codes below.

PA:



[MedlinePlus](#)



[NBSIC](#)



[Organic Acidemia Association](#)

MMA:



[MedlinePlus](#)



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