

Newborn Screening ACT Sheet

[Elevated C5 Acylcarnitine]

Isovaleric Acidemia

Differential Diagnosis: Isovaleric acidemia (IVA), 2-Methylbutyrylglycinuria (2MBG) (also referred to as short/branched chain acyl-CoA dehydrogenase deficiency or SBCAD deficiency); antibiotic-related (pivalic acid derived) artifact.

Condition Description: IVA and 2MBG result from different defects in the metabolism of the branched chain amino acids, leucine (isovaleryl-CoA dehydrogenase in IVA) and isoleucine (short/branched chain acyl-CoA dehydrogenase in 2MBG). In both conditions specific metabolites accumulate and are potentially toxic.

Take the Following **IMMEDIATE** Actions

- Contact family to inform them of the newborn screening result and ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).
- Consult with pediatric metabolic specialists
- Evaluate the newborn; if 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 metabolic acidosis (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).
- Report findings to newborn screening program.

Diagnostic Evaluation: Plasma acylcarnitine analysis confirms the increased C5. Urine organic acid analysis will show isovalerylglycine in IVA and 2-methylbutyrylglycine in most cases of 2MBG. Urine acylglycine and acylcarnitine analysis may also be informative.

Clinical Considerations: Isovaleric acidemia presents in the neonate with metabolic ketoacidosis, a “sweaty feet” odor, dehydration, hyperammonemia, ketonuria, vomiting, hypoglycemia, and failure to thrive. Milder variants without neonatal illness exist. Long term prognosis of IVA with appropriate therapy is good. The clinical spectrum of 2MBG is variable. To date, most patients identified by newborn screening with 2MBG are of Hmong descent and remain asymptomatic.

Additional Information:

(Click on the name to take you to the website. Complete URLs are listed in the Appendix)

[New England Consortium of Metabolic Programs](#)

[IVA Emergency Protocol](#)

[Gene Tests](#)

[Genetics Home Reference](#)

Referral (local, state, regional and national):

[Testing](#)

[Clinical](#)

Disclaimer: These standards and guidelines are designed primarily as an educational resource for physicians to help them provide quality medical services. Adherence to these standards and guidelines does not necessarily ensure a successful medical outcome. These standards and guidelines 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 healthcare provider should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen. It may be prudent, however, to document in the patient's record the rationale for any significant deviation from these standards and guidelines.

APPENDIX: Resources with Full URL Addresses

Additional Information:

New England Consortium of Metabolic Programs

http://www.childrenshospital.org/newenglandconsortium/NBS/IVA/IVA_protocol.htm

IVA Emergency Protocol

<http://www.childrenshospital.org/newenglandconsortium/NBS/ISOVAL.html>

Gene Tests

<http://www.genetests.org/servlet/access?db=geneclinics&site=gt&id=8888891&key=TQVVBlc6UfmSh&gry=&fcn=y&fw=Qvcz&filename=/profiles/oa-overview/index.html>

Genetics Home Reference <http://ghr.nlm.nih.gov/condition=isovalericacidemia>

Referral (local, state, regional and national):

Testing <http://biochemgen.ucsd.edu/UCSDW3BG/Labchoose.asp>

http://genetests.org/servlet/access?prg=j&db=genetests&site=gt&id=8888891&fcn=c&qry=2251&res=nous&res=nointl&key=gYE3unrxIzSww&show_flag=c

Clinical

<http://www.genetests.org/servlet/access?id=8888891&key=RRqZcXXEUiAx9&fcn=y&fw=zLsf&filename=/clinicsearch/searchclinic.html>

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