

ACT Sheet

Newborn Screening ACT Sheet

[Elevated C5 Acylcarnitine]

Isovaleric Acidemia

Differential Diagnosis: Isovaleric acidemia (IVA), short/branched chain acyl-CoA dehydrogenase (SBCAD) deficiency, medication artifact.

Condition Description: IVA and SBCAD are organic acid disorders resulting from defects in the metabolism of leucine (isovaleryl-CoA dehydrogenase deficiency in IVA) or isoleucine (short/branched-chain acyl-CoA dehydrogenase deficiency in SBCAD). In both conditions, specific metabolites accumulate which produce toxicity, particularly in IVA.

You Should Take the Following <u>IMMEDIATE</u> Actions:

- Inform family of the newborn screening result.
- Ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea, odor of sweaty feet).
- Consult with pediatric metabolic specialist the same day.
- Evaluate the newborn (poor feeding, vomiting, lethargy, tachypnea). If any of these signs are present, or if 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 specialist.
- Provide family with basic information about the possible diagnoses and their management.
- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: <u>Plasma acylcarnitine profile</u>: C5 is elevated in IVA and SBCAD. <u>Urine organic acids</u>: Isovalerylglycine is elevated in IVA, and 2-methylbutyrylglycine (2MBG) is elevated in SBCAD. <u>Urine acylglycines</u> may be more sensitive in detecting 2MBG elevations in SBCAD. <u>Molecular genetic testing</u>: can be used to confirm the diagnosis.

Clinical Considerations: Isovaleric acidemia presents in the neonate with lethargy, poor feeding, vomiting, "sweaty feet" odor, metabolic ketoacidosis, hyperammonemia, hypoglycemia, and neutropenia. Milder variants without neonatal illness can occur. Treatment should be initiated under the guidance of a specialist and includes the avoidance of fasting, protein restriction and supplementation with L-carnitine. The prognosis of IVA with appropriate therapy is good. Most patients identified by newborn screening with SBCAD remain asymptomatic.

Additional Information:

How to Communicate Newborn Screening Results Emergency Protocols (New England Consortium of Metabolic Programs) GARD Medline Plus Condition Information for Families- HRSA Newborn Screening Clearinghouse

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

Find a Genetics Clinic Directory Genetic Testing Registry

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.

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State and Other Resources

State Newborn Screening Program

Newborn Screening, State of Rhode Island Department of Health 401-921-7619, health.ri.gov/newbornscreening/

Genetics/Metabolic Consultants

Division of Genetics, Lifespan Physician's Group, Hasbro Children's Hospital 401-444-4000, www.lifespan.org/centers-services/childrens-neurodevelopmentcenter/genetics-and-dysmorphology

Information for Clinicians and Families

Rhode Island Medical Home Portal (see Newborn Disorders and Parents & Families sections) ri.medicalhomeportal.org/newborn/isovaleric-acidemia

Parent/Family Support

Organic Acidemia Association www.oaanews.org/iva.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/achdnccommunication-guide-newborn.pdf

Emergency Protocols (New England Consortium of Metabolic Programs) www.newenglandconsortium.org/isova

GARD (Genetic and Rare Diseases Information Center) rarediseases.info.nih.gov/diseases/465/isovaleric-acidemia

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

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

Referral (local, state, regional and national)

Find a Genetics Clinic Directory clinics.acmg.net

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

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