ACMG
American College of Medical Genetics and Genomics
Translating Genes Into Health®

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 IMMEDIATE 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: Plasma acylcarnitine profile: C5 is elevated in IVA and SBCAD. Urine organic acids: Isovalerylglycine is elevated in IVA, and 2-methylbutyrylglycine (2MBG) is elevated in SBCAD. Urine acylglycines may be more sensitive in detecting 2MBG elevations in SBCAD. Molecular genetic testing: 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

 (Funded in part through MCHB/HRSA/HHS grant #U22MC03957;#UH9MC30770; National Coordinating Center for the Regional Genetics Networks)

State and Other Resources

State Newborn Screening Program

Newborn Screening Program, Utah Department of Health and Human Services
801-584-8256, newbornscreening.health.utah.gov/

Genetics/Metabolic Consultants

Pediatric Medical Genetics, University of Utah Department of Pediatrics
801-213-3599, healthcare.utah.edu/pediatrics/programs-services/genetics.php

Information for Clinicians and Families

Utah Medical Home Portal (see Newborn Disorders and Parents & Families sections)
ut.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/achdnc-communication-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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