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

ACT Sheet

Newborn Screening ACT Sheet

[Elevated C4 Acylcarnitine]

Short-Chain Acyl-CoA Dehydrogenase (SCAD) Deficiency

Differential Diagnosis: Short-chain acyl CoA dehydrogenase (SCAD) deficiency; Isobutyryl-CoA dehydrogenase (IBDH) deficiency (also known as isobutyrylglycinuria (IBG)); ethylmalonic encephalopathy (EE).

Condition Description: SCAD deficiency disrupts fatty acid oxidation at the level of short chain fatty acids, leading to elevated C4 acylcarnitine (as butyrylcarnitine). IBDH is a disorder of valine metabolism leading to elevated C4 acylcarnitine (as isobutyrylcarnitine). Both conditions have limited, if any, clinical significance. EE is a disorder caused by variants in a gene coding for a mitochondrial enzyme. In EE, potentially toxic metabolites accumulate preventing the mitochondria from producing energy.

You Should Take the Following Actions:

- Inform family of the newborn screening result.
- Ascertain clinical status (typically asymptomatic; rarely lethargy, hypotonia, vomiting).
- Consult with pediatric metabolic specialist.
- Evaluate newborn for signs of hypoglycemia, lethargy, or metabolic acidosis. If any of these findings are present or if the newborn is ill, transport to a hospital for further treatment in consultation with a metabolic specialist.
- Initiate confirmatory diagnostic testing and management, as recommended by the specialist.
- Provide the family with basic information about these conditions and their management.

- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: **Plasma acylcarnitines:** C4 is elevated in both SCAD and IBDH deficiencies. C4 (+/- C5) is elevated in EE. **Urine organic acids** demonstrate elevated ethylmalonic acid in SCAD and isobutyrylglycine in IBDH deficiency. EE is associated with elevated ethylmalonic acid and mild elevations of glycine conjugates. **Molecular genetic testing** may be required to differentiate these disorders.

Clinical Considerations: SCAD deficiency and IBDH deficiencies are typically benign. EE can present in infancy with developmental delay, diarrhea and petechiae.

Additional Information:

How to Communicate Newborn Screening Results
Emergency Protocols (New England Consortium of Metabolic Programs)
Gene Reviews (SCAD | EE)
Medline Plus (SCAD | EE | IBDH)
Condition Information for Families- HRSA Newborn Screening Clearinghouse (SCAD | EE | IBDH)

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

Metabolic (Bloodspot) Screening, Montana's Newborn Screening Programs
406-444-0984, dphhs.mt.gov/ecfsd/cshs/newbornscreeningprograms/

Short-term Follow-up Coordinator - Crystal Fortune, MT Laboratory Services Bureau
406-444-0930 or 800-821-7284 cfortune@mt.gov

Genetics/Metabolics Consultants

Shodair Children's Hospital Medical Genetics Staff will contact you with recommendations.
Metabolic Clinic: 406-444-1099; Clinics held across Montana: 406-444-1016
shodair.org/about-shodair/contact/

If emergency consultation with a metabolic specialist is necessary, contact One Call (24/7) at Children's Hospital Colorado (800-525-4871) and ask to speak to the metabolic specialist on call.

Information for Clinicians and Families

Montana Medical Home Portal (see Newborn Disorders and Parents & Families sections)
mt.medicalhomeportal.org/newborn/short-chain-acyl-coa-dehydrogenase-deficiency

Parent/Family Support

FOD Family Support Group – fodsupport.org/

United Mitochondrial Disease Foundation – www.umdf.org

Organic Acidemia Association – www.oaanews.org/

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/scadd

Gene Reviews
- www.ncbi.nlm.nih.gov/books/NBK63582/
- www.ncbi.nlm.nih.gov/books/NBK453432/

Medline Plus
- medlineplus.gov/genetics/condition/short-chain-acyl-coa-dehydrogenase-deficiency/
- medlineplus.gov/genetics/condition/ethylmalonic-encephalopathy/
- medlineplus.gov/genetics/condition/isobutyryl-coa-dehydrogenase-deficiency/

Condition Information for Families-HRSA Newborn Screening Clearinghouse
- newbornscreening.hrsa.gov/conditions/short-chain-acyl-coa-dehydrogenase-deficiency
- newbornscreening.hrsa.gov/conditions/ethylmalonic-encephalopathy
- newbornscreening.hrsa.gov/conditions/isobutyryl-coa-dehydrogenase-deficiency

Referral (local, state, regional and national)

Find a Genetics Clinic Directory
clinics.acmg.net

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