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)

Local Resources *(Insert Local Website Links)*

State Resource Site (Insert Website Information)

Name	
URL	
Comments	

Local Resource Site (Insert Website Information)

Name	
URL	
Comments	

Appendix *(Resources with Full URL Addresses)*

Additional Information

How to Communicate Newborn Screening Results

- https://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)

- https://www.newenglandconsortium.org/scadd

Gene Reviews

- https://www.ncbi.nlm.nih.gov/books/NBK63582/
- https://www.ncbi.nlm.nih.gov/books/NBK453432/

Medline Plus

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

Condition Information for Families-HRSA Newborn Screening Clearinghouse

- https://newbornscreening.hrsa.gov/conditions/short-chain-acyl-coa-dehydrogenase-deficiency
- https://newbornscreening.hrsa.gov/conditions/ethylmalonic-encephalopathy
- https://newbornscreening.hrsa.gov/conditions/isobutyryl-coa-dehydrogenase-deficiency

Referral (local, state, regional and national)

Find a Genetics Clinic Directory

- https://clinics.acmg.net

Genetic Testing Registry

- https://www.ncbi.nlm.nih.gov/gtr/

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