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

ACT Sheet

Newborn Screening ACT Sheet

[Increased Leucine]

Maple Syrup Urine Disease

Differential Diagnosis: Maple syrup urine disease (MSUD); hydroxyprolinemia.

Condition Description: In MSUD, leucine, isoleucine, alloisoleucine, and valine (branched-chain amino acids) cannot be metabolized beyond their α-ketoacid intermediates (due to a block in the shared catabolic pathway). Branched-chain amino acids and branched-chain ketoacids accumulate and produce severe toxicity often within the first 48 hours of life.

You Should Take the Following IMMEDIATE Actions:

- Inform family of the newborn screening result.
- Ascertain clinical status (poor feeding, vomiting, lethargy, tachypnea).
- Consult with pediatric metabolic specialist the same day.
- Evaluate the newborn for signs of poor feeding, lethargy, tachypnea, alternating hypertonia/hypotonia, or seizures. If any of these findings 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 the specialist.
- Provide the family with basic information about MSUD, including dietary management.

- Report final diagnostic outcome to newborn screening program.

Diagnostic Evaluation: In MSUD, plasma amino acid analysis demonstrates elevations of leucine, isoleucine, alloisoleucine, and valine (the branched-chain amino acids), and urine organic acid analysis reveals elevated branched-chain alpha-hydroxy- and alpha-keto-acids. In newborn screening, leucine, isoleucine, alloisoleucine, and hydroxyproline are not differentiated: if the newborn has hydroxyprolinemia, confirmatory amino acid analysis will only show increased hydroxyproline.

Clinical Considerations: MSUD presents in the neonate with feeding intolerance, failure to thrive, vomiting, lethargy, and maple syrup odor, particularly in urine and cerumen. If untreated, the condition will rapidly progress to seizures, coma, cerebral edema, irreversible developmental delay, and possibly death. Individuals with variant forms of MSUD may not present with clinical symptoms until later in infancy or childhood but remain at risk for severe metabolic decompensation. Hydroxyprolinemia is a benign condition.

Additional Information:

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

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

Find a Genetics Clinic Directory
Genetic Testing Registry

State and Other Resources

State Newborn Screening Program

Nevada Newborn Screening Program, Nevada State Public Health Laboratory
775-682-6238, med.unr.edu/nsphl/newborn-screening

Genetics/Metabolic Consultants

Nicola Longo, MD, PhD, University of Utah Genetics/Pediatrics
801-585-2457, healthcare.utah.edu/fad/mddetail.php?physicianID=u0305101

Information for Clinicians and Families

Nevada Medical Home Portal (see Newborn Disorders and Parents & Families sections)
nv.medicalhomeportal.org/newborn/maple-syrup-urine-disease

Parent/Family Support

Maple Syrup Urine Disease Family Support Group (National)
msud-support.org/contacts/

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/msud

Gene Reviews
www.ncbi.nlm.nih.gov/books/NBK1319/

Medline Plus
medlineplus.gov/genetics/condition/maple-syrup-urine-disease/

Condition Information for Families-HRSA Newborn Screening Clearinghouse
newbornscreening.hrsa.gov/conditions/maple-syrup-urine-disease

Referral (local, state, regional and national)

Find a Genetics Clinic Directory
clinics.acmg.net

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