Maple Syrup Urine Disease: Allo-isoleucine and Branched-Chain Amino Acids, Quantitative, Dried Blood Spot

**Condition Description**

Maple Syrup Urine Disease (MSUD) is an organic aciduria that is caused by the inability to break down branch-chain amino acids, leucine, isoleucine, and valine. The resulting build-up of these amino acids results in:

- vomiting
- dehydration
- severe metabolic acidosis
- characteristic maple syrup odor of the sweat and urine

MSUD is among the disorders tested for by newborn screening and is treatable by dietary modification. MSUD affects between 1 in 125,000-300,000 people in the general population. MSUD is common in the Old Order Mennonite population of southeastern Pennsylvania, occurring in 1 in 760 live births. MSUD is inherited in an autosomal recessive manner, therefore the recurrence risk for carrier parents of an affected child is 1 in 4.

MSUD is suggested by biochemical analysis of allo-isoleucine and branched chain amino acids, by liquid chromatography - tandem mass spectrometry (LC-MS/MS), or by amino acid analyzer; urine organic acids by gas chromatography/mass spectrometry (GC/MS). MSUD can be diagnosed biochemically by assaying BCKD activity in cultured skin fibroblasts or transformed leukocytes.

MSUD is caused by deficient activity of the branched-chain alpha-keto acid dehydrogenase (BCKD) complex. The BCKD complex consists of three subunits: the 2-oxoisovaleratedehydrogenase alpha subunit (E1 alpha), 2-oxoisovalerate dehydrogenase beta subunit (E1 beta) and lipoamide acyltransferase component (E2). Patients with MSUD may have mutations in the BCKDHA (19q13), BCKDHB (6p21), or DBT gene (1p31), which encode the E1 alpha, E1 beta, and DBT subunits of BCKD complex, respectively.

Dietary monitoring is recommended by plasma amino acids or dried blood spot allo-isoleucine.

Please [click here](#) for the GeneReviews summary on MSUD.

**Indications**

Second-tier test for patients with abnormal newborn screen results, BCAA elevations, and dietary monitoring of patients with maple syrup urine disease (MSUD).

**Methodology**

Liquid Chromatography-Tandem Mass spectrometry (LC-MS/MS)

Stable Isotope Dilution Analysis

**Detection**

Allo-isoleucine is nearly undetectable in individuals not affected by MSUD. Accordingly, its presence is diagnostic for MSUD, and its absence is sufficient to rule out classic MSUD.

**Reference Range**

Reported in milligrams percent and micromoles. The concentration of leucine is used as monitoring parameter for MSUD patients. The therapeutic range of Leu for MSUD is: 2-6 mg percent.

Reference ranges:
- Allo-isoleucine < 2 umol/L
- Leucine 35 - 215 umol/L
- Isoleucine 13 - 130 umol/L
- Valine 51 - 325 umol/L

**Specimen Requirements**

*Submit only 1 of the following specimen types*

**Type:** Dried Blood Spot

**Specimen Requirements:**
Filter Paper
Peripheral blood from finger prick or heel stick spotted on filter paper, completely saturating the circle. Air dry the sample.

**Specimen Collection and Shipping:**

Disclaimer: This information is confidential and subject to change without notice. It may not be reproduced in whole or part unless authorized in writing by an authorized EGL representative.
Do not expose specimen to heat or direct sunlight. Keep the specimen dry. Ship sample at room temperature with overnight delivery.

**Special Instructions**

- Do not expose specimen to heat or direct sunlight
- Do not stack wet specimens
- Do not use device or capillary containing EDTA to collect specimen
- Keep the specimen dry

**Related Tests**

- Organic Acids Quantitative Analysis (OA)
- Amino Acids Analysis, Plasma (AA)
- MSUD sequencing (SB) and deletion/duplication (NI)