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

Test Code: BMSUD  
Turnaround time: 7 days  
CPT Codes: 82136 x1

**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**

**Type: Dried Blood Spot**

Specimen Requirements:

Peripheral blood from finger prick or heel stick spotted on filter paper, completely saturating the circle. Air dry sample.

Specimen Collection and Shipping: 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)