

**The New Jersey Department of Health and Senior Services  
Newborn Screening and Genetic Services**

## **Maple Syrup Urine Disease (MSUD)**

### **Information for Health Professionals**

#### **Description**

Maple Syrup Urine Disease (MSUD) is a rare disorder of catabolism of the branched chain amino acids (BCAAs) causing elevated quantities of leucine, isoleucine and valine and their respective branched chain ketoacids (BCKA) to accumulate in body fluids. In MSUD the ingestion of BCAAs exceeds the metabolic requirements for growth, and catabolism of the excess amino acids is blocked, thus, the BCAA and BCKA accumulate in the blood (to toxic levels) and are excreted in the urine. As with virtually all hereditary disorders, there are less severe variants, the mildest of which may go undetected for some time until some intercurrent illness unmasks the biochemical abnormalities.

#### **Incidence**

MSUD has been found in peoples all over the world but is most prevalent among the Old Order Mennonite population in Lancaster, Pennsylvania. Its occurrence is also higher in countries in which consanguineous marriage is common. The birth incidence rate is approximately 1:290,000 (Old Order Mennonites, 1:760).

#### **Clinical Features**

Infants with MSUD appear normal at birth, but they usually remain well for only a few days. Symptoms are usually concomitant with the ingestion of dietary protein. They progress from poor feeding and vomiting to lethargy and coma. A high-pitched cry, irritability, convulsions, spasticity, and central nervous system depression are additional presenting signs, with severe metabolic acidosis and hypoglycemia. Plasma leucine begins to rise, usually within 24 hours of birth, and within a few days ketoacids appear in the urine. These impart a characteristic sweet maple syrup odor to the urine, which gives the disease its name. Even in the mildest form, MSUD can result in mental retardation.

#### **Screening**

The screening test for MSUD is done by the IEM laboratory as part of the standard newborn biochemical screening. Tandem mass spectrometry (MS/MS) is applied to this process.

#### **Confirmatory Testing**

It is important to remember that newborn biochemical screening is just a screening test, and a diagnosis must be confirmed using an independent

analysis of blood and urine for amino acids as well as other appropriate tests. It is essential to confirm or exclude the diagnosis of MSUD in a timely fashion and with a high degree of accuracy to avoid unnecessary testing, to provide appropriate interventions, prognostic and genetic counseling, and to ensure access to specialized medical services.

**It is strongly recommended that any baby suspected of having this disorder be evaluated as quickly as possible by a metabolic/genetic specialist who is experienced in the diagnosis and treatment of babies with MSUD, since confirmatory testing and management are complicated and death may occur rapidly in untreated cases.**

### **Treatment**

Treatment, which must be continued for life, is a strict diet designed to control the intake of branched chain amino acids. Since this requires strict compliance with a special diet, close supervision by a dietician and a metabolic/genetic specialist is essential. Frequent blood testing of amino acids allows for the adjusting of the branched chain amino acids so that they are neither deficient nor in excess.

Most forms of the disease, if left untreated, may result in life threatening neurological damage or death within a few days to a few weeks. Milder variants should have better outcomes with early identification. Normal development and neurologic outcomes have been observed in babies begun on treatment prior to symptoms.

### **Implications for Genetic Counseling**

MSUD is inherited in an autosomal recessive manner. Therefore, a negative family history does not exclude the possibility of this diagnosis. Genetic counseling is also suggested for prospective parents with a family history of maple syrup urine disease.

### **Interpretations/Recommendations**

#### **Expected Results:**

- **<325  $\mu$ M Leucine plus Leucine/Alanine ratio <2.25 and Leucine/Phenylalanine ratio <8**
- **Within Acceptable Limits**

#### **Equivocal Results:**

- **$\geq$ 325-499  $\mu$ M Leucine plus Leucine/Alanine ratio <2.25 and Leucine/Phenylalanine ratio <8**
- **Recommend: Repeat filter paper sample within 2 days**

## Interpretations/Recommendations (cont.)

### Repeat equivocal results:

- Becomes a presumptive positive
- Recommend: Immediate assessment of baby's health and consultation with a metabolic/genetic specialist strongly recommended

### Presumptive-Positive Results- initial or repeat specimen:

- $<325 \mu\text{M}$  Leucine plus Leucine/Alanine ratio  $\geq 2.25$  and Leucine/Phenylalanine ratio  $\geq 8$
- $\geq 325\text{-}399 \mu\text{M}$  Leucine plus Leucine/Alanine ratio  $\geq 2.25$  and/or Leucine/ $\mu$ Phenylalanine ratio  $\geq 8$
- $\geq 400\text{-}499 \mu\text{M}$  Leucine plus Leucine/Alanine ratio  $\geq 2.25$  and/or Leucine/Phenylalanine ratio  $\geq 8$
- $\geq 500 \mu\text{M}$  Leucine, regardless of ratios
- **Recommend (for all presumptive positives):** Immediate assessment of baby's health and consultation with metabolic/genetic specialist strongly recommended.

**Note:** Newborn screening is an adjunct to clinical assessment, which is paramount. Maple Syrup Urine Disease should be considered in infants with any of the signs/symptoms.

Additional information:

eMedicine

<http://www.emedicine.com/ped/topic1368.htm>

Gene Tests/Gene Clinics

<http://www.genetests.org>

Illinois Department of Public Health Newborn Screening Program

<http://www.idph.state.il.us/HealthWellness/fs/msud.htm>

For questions, contact:

Inborn Errors of Metabolism Laboratory at (609) 292-3090

Newborn Screening and Genetic Services Program at (609) 292-1582

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