



What is Maple Syrup Urine Disease?

Maple syrup urine disease (MSUD) is an inherited metabolic disease. When untreated, the classic form of MSUD is characterized by life threatening complications in the newborn period, including poor feeding, vomiting, lethargy, developmental delay, and a distinctive sweet odor in the urine. It involves abnormalities in an enzyme complex that is responsible for breaking down the amino acids leucine, isoleucine, and valine. The symptoms of MSUD are due to the toxic build-up of these amino acids and their metabolites in the body, especially affecting the nervous system. MSUD is also known as branched-chain ketoaciduria, BCKD deficiency, and it is also known by its subtypes: MSUD type 1A, 1B, and 2.¹

What are the symptoms of Maple Syrup Urine Disease and what treatment is available?

Maple syrup urine disease can vary in age of onset and severity. Classic MSUD is the severe and most common form of the disease. It presents soon after birth with symptoms that may include¹:

- A distinctive sweet, maple syrup odor of the ear wax and urine
- Distinctive movements and abnormal muscle contractions known as “bicycling” and “fencing”
- Poor feeding
- Lethargy (lack of energy)
- Irritability
- Difficulty breathing
- Brain swelling

If untreated, symptoms worsen, and coma and possible death may occur within the first two weeks of life.¹

Less severe forms of MSUD may occur in infancy, childhood, or periodically throughout life. Symptoms may be similar to the classic form and include feeding problems, poor growth, developmental delays, risk of brain swelling, and psychological problems. Episodes of decompensation (severe symptoms requiring intensive care) may occur after illness, infections, or fever.¹

There is no cure for any form of MSUD, but available treatments for MSUD include a low-protein diet and nutritional supplements throughout life. Treatment can result in dramatic improvement of disease; however, individuals with MSUD remain at an increased risk for episodes of decompensation. Liver transplantation is sometimes considered for individuals with classic MSUD.¹

Maple syrup urine disease is included on newborn screening panels in all 50 states.²

How is Maple Syrup Urine Disease inherited?

MSUD is an autosomal recessive disease caused by mutations in three genes. Mutations in the *BCKDHA* (MSUD type 1A) or *BCKDHB* (MSUD type 1B) genes account for approximately 80% of cases. Mutations in the *DBT* (MSUD type 2) gene are responsible for the remaining cases.¹ The InheriTest Carrier Screen evaluates mutations in the *BCKDHA* and *BCKDHB* genes.

An individual who has only one mutation in any of these genes is a “carrier” and is not expected to have related health problems. An individual who inherits two mutations in the same gene, one from each parent, is expected to be affected with MSUD. For example, a child with two *BCKDHA* mutations would have MSUD, but a child with one *BCKDHA* mutation and one *BCKDHB* mutation would only be a carrier.





If both members of a couple are carriers of a mutation in the same gene, the risk of having an affected child is 25% in each pregnancy; therefore, it is especially important that the reproductive partner of a carrier be offered testing.

Who is at risk for Maple Syrup Urine Disease?

Maple syrup urine disease can occur in individuals of all races and ethnicities. MSUD type 1A is more common in Mennonite individuals, and MSUD type 1B is more common in individuals of Ashkenazi (Eastern European) Jewish ancestry. ^{1,4}

Carrier Frequencies for Select Ethnic Groups

Population	Type	Carrier Frequency
Mennonite*	MSUD type 1A	1 in 13 ³
General	MSUD type 1A	1 in 321 ¹
Ashkenazi Jewish	MSUD type 1B	1 in 97 ⁴

*Old Order Mennonites of southeastern Pennsylvania and derivative settlements ³

Having a relative who is a carrier or who is affected can increase an individual's risk of being a carrier. Consultation with a genetics health professional may be helpful in determining carrier risk and appropriate testing.

What does a positive test result mean?

If a gene mutation is identified, an individual should speak to a physician or genetics health professional about the implications of the result and appropriate testing for the reproductive partner and at-risk family members.

What does a negative test result mean?

A negative result reduces, but does not eliminate, the possibility that an individual carries a gene mutation. The likelihood of being a carrier is also influenced by family history, medical symptoms, and other relevant test results.

Where can I get more information?

- MSUD family support group: <http://www.msud-support.org/>
- Screening, Technology and Research in Genetics: <http://www.newbornscreening.info/Parents/aminoaciddisorders/MSUD.html>

References

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2. National Newborn Screening Status Report: Updated 2/15/12. Available at <http://genes-r-us.uthscsa.edu/nbsdisorders.pdf>.
3. Puffenberger EG. Genetic heritage of the Old Order Mennonites of Southeastern Pennsylvania. *Am. J. Med. Genet. Part C (Semin. Med. Genet.)* 2003; 121C: 18-31.
4. Scott, SA et al. Experience with Carrier Screening and Prenatal Diagnosis for 16 Ashkenazi Jewish Genetic Diseases *Hum Mut* 2010; 31:1240-1250.

