



maple syrup urine disease

Maple syrup urine disease is an inherited disorder in which the body is unable to process certain protein building blocks (amino acids) properly. The condition gets its name from the distinctive sweet odor of affected infants' urine. It is also characterized by poor feeding, vomiting, lack of energy (lethargy), abnormal movements, and delayed development. If untreated, maple syrup urine disease can lead to seizures, coma, and death.

Maple syrup urine disease is often classified by its pattern of signs and symptoms. The most common and severe form of the disease is the classic type, which becomes apparent soon after birth. Variant forms of the disorder become apparent later in infancy or childhood and are typically milder, but they still lead to delayed development and other health problems if not treated.

Frequency

Maple syrup urine disease affects an estimated 1 in 185,000 infants worldwide. The disorder occurs much more frequently in the Old Order Mennonite population, with an estimated incidence of about 1 in 380 newborns.

Genetic Changes

Mutations in the *BCKDHA*, *BCKDHB*, and *DBT* genes can cause maple syrup urine disease. These three genes provide instructions for making proteins that work together as part of a complex. The protein complex is essential for breaking down the amino acids leucine, isoleucine, and valine, which are present in many kinds of food, particularly protein-rich foods such as milk, meat, and eggs.

Mutations in any of these three genes reduce or eliminate the function of the protein complex, preventing the normal breakdown of leucine, isoleucine, and valine. As a result, these amino acids and their byproducts build up in the body. Because high levels of these substances are toxic to the brain and other organs, their accumulation leads to the serious health problems associated with maple syrup urine disease.

Researchers are studying other genes related to the same protein complex that may also be associated with maple syrup urine disease.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal

recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- BCKD deficiency
- branched-chain alpha-keto acid dehydrogenase deficiency
- branched-chain ketoaciduria
- ketoacidemia
- MSUD

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Increased leucine
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/Leucine.pdf>

Formal Treatment/Management Guidelines

- British Inherited Metabolic Disease Group: MSUD Clinical Management Guidelines
http://www.bimdg.org.uk/store/enbs//Final_MSUD_clinical_management_guidelines_v11_Jan_2017_647074_25042017.pdf
- British Inherited Metabolic Disease Group: MSUD Dietetic Management Pathway
http://www.bimdg.org.uk/store/enbs//MSUD_Dietetic_management_pathway_April_2015_660203_12052015.pdf
- New England Consortium of Metabolic Programs: Acute Illness Protocol
<http://newenglandconsortium.org/for-professionals/acute-illness-protocols/organic-acid-disorders/maple-syrup-urine-disease-msud/>

Genetic Testing

- Genetic Testing Registry: Classical maple syrup urine disease
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268568/>
- Genetic Testing Registry: Intermediate maple syrup urine disease
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1621920/>
- Genetic Testing Registry: Maple syrup urine disease
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0024776/>

Other Diagnosis and Management Resources

- Baby's First Test
<http://www.babysfirsttest.org/newborn-screening/conditions/maple-syrup-urine-disease-msud>
- GeneReview: Maple Syrup Urine Disease
<https://www.ncbi.nlm.nih.gov/books/NBK1319>
- MedlinePlus Encyclopedia: Maple Syrup Urine Disease
<https://medlineplus.gov/ency/article/000373.htm>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Encyclopedia: Maple Syrup Urine Disease
<https://medlineplus.gov/ency/article/000373.htm>
- Health Topic: Amino Acid Metabolism Disorders
<https://medlineplus.gov/aminoacidmetabolismdisorders.html>
- Health Topic: Genetic Brain Disorders
<https://medlineplus.gov/geneticbraindisorders.html>
- Health Topic: Newborn Screening
<https://medlineplus.gov/newbornscreening.html>

Genetic and Rare Diseases Information Center

- Maple syrup urine disease
<https://rarediseases.info.nih.gov/diseases/3228/maple-syrup-urine-disease>

Educational Resources

- Disease InfoSearch: Maple syrup urine disease
<http://www.diseaseinfosearch.org/Maple+syrup+urine+disease/4453>
- Genetic Science Learning Center, University of Utah
<http://learn.genetics.utah.edu/content/disorders/singlegene/>
- Illinois Department of Public Health Genetics and Newborn Screening Program
<http://www.idph.state.il.us/HealthWellness/fs/msud.htm>
- MalaCards: intermediate maple syrup urine disease
http://www.malacards.org/card/intermediate_maple_syrup_urine_disease
- MalaCards: maple syrup urine disease mild variant
http://www.malacards.org/card/maple_syrup_urine_disease_mild_variant
- Merck Manual Consumer Version: Disorders of Amino Acid Metabolism
<http://www.merckmanuals.com/home/children-s-health-issues/hereditary-metabolic-disorders/disorders-of-amino-acid-metabolism>
- Michigan Department of Community Health
http://www.michigan.gov/documents/msud_79207_7.pdf
- My46 Trait Profile
<https://www.my46.org/trait-document?trait=Maple%20syrup%20urine%20disease&type=profile>
- New England Consortium of Metabolic Programs
<http://newenglandconsortium.org/for-families/other-metabolic-disorders/organic-acid-disorders/msud/>
- Orphanet: Classic maple syrup urine disease
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=268145
- Orphanet: Intermediate maple syrup urine disease
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=268162
- Orphanet: Maple syrup urine disease
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=511
- Screening, Technology, and Research in Genetics
<http://www.newbornscreening.info/Parents/aminoaciddisorders/MSUD.html>
- Virginia Department of Health
http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_MSUD_English.pdf
- Washington State Department of Health
<http://www.doh.wa.gov/Portals/1/Documents/5220/5220-MSUD-GO.pdf>

Patient Support and Advocacy Resources

- CLIMB: Children Living with Inherited Metabolic Diseases (UK)
<http://www.climb.org.uk/>
- MSUD Family Support Group
<http://www.msud-support.org/>
- National Organization for Rare Disorders
<https://rarediseases.org/rare-diseases/maple-syrup-urine-disease/>
- Organic Acidemia Association
<http://www.oaanews.org/>
- Resource List from the University of Kansas Medical Center
<http://www.kumc.edu/gec/support/maple.html>

GeneReviews

- Maple Syrup Urine Disease
<https://www.ncbi.nlm.nih.gov/books/NBK1319>

ClinicalTrials.gov

- ClinicalTrials.gov
<https://clinicaltrials.gov/ct2/results?cond=%22Maple+Syrup+Urine+Disease%22+OR+%22maple+syrup+urine+disease%22>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Maple+Syrup+Urine+Disease%5BMAJR%5D%29+AND+%28maple+syrup+urine+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

OMIM

- MAPLE SYRUP URINE DISEASE
<http://omim.org/entry/248600>
- MAPLE SYRUP URINE DISEASE, MILD VARIANT
<http://omim.org/entry/615135>

MedGen

- Classical maple syrup urine disease
<https://www.ncbi.nlm.nih.gov/medgen/78689>
- Intermittent maple syrup urine disease
<https://www.ncbi.nlm.nih.gov/medgen/78690>

- Maple syrup urine disease
<https://www.ncbi.nlm.nih.gov/medgen/6217>
- Mild maple syrup urine disease
<https://www.ncbi.nlm.nih.gov/medgen/541364>

Sources for This Summary

- Burrage LC, Nagamani SC, Campeau PM, Lee BH. Branched-chain amino acid metabolism: from rare Mendelian diseases to more common disorders. *Hum Mol Genet.* 2014 Sep 15;23(R1):R1-8. doi: 10.1093/hmg/ddu123. Epub 2014 Mar 20. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/24651065>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4170715/>
- Carleton SM, Peck DS, Grasela J, Dietiker KL, Phillips CL. DNA carrier testing and newborn screening for maple syrup urine disease in Old Order Mennonite communities. *Genet Test Mol Biomarkers.* 2010 Apr;14(2):205-8. doi: 10.1089/gtmb.2009.0107.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/20136525>
- GeneReview: Maple Syrup Urine Disease
<https://www.ncbi.nlm.nih.gov/books/NBK1319>
- Harris-Haman P, Brown L, Massey S, Ramamoorthy S. Implications of Maple Syrup Urine Disease in Newborns. *Nurs Womens Health.* 2017 Jun - Jul;21(3):196-206. doi: 10.1016/j.nwh.2017.04.009.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/28599741>
- Oyarzabal A, Martínez-Pardo M, Merinero B, Navarrete R, Desviat LR, Ugarte M, Rodríguez-Pombo P. A novel regulatory defect in the branched-chain α -keto acid dehydrogenase complex due to a mutation in the PPM1K gene causes a mild variant phenotype of maple syrup urine disease. *Hum Mutat.* 2013 Feb;34(2):355-62. doi: 10.1002/humu.22242. Epub 2012 Dec 12.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/23086801>
- Simon E, Flaschker N, Schadewaldt P, Langenbeck U, Wendel U. Variant maple syrup urine disease (MSUD)--the entire spectrum. *J Inherit Metab Dis.* 2006 Dec;29(6):716-24. Epub 2006 Oct 25.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17063375>

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