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_v12_Mar_2018_975057_02032018.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
  https://www.merckmanuals.com/home/children-s-health-issues/hereditary-metabolic-disorders/overview-of-amino-acid-metabolism-disorders
- Michigan Department of Community Health
  https://www.michigan.gov/documents/msud_79207_7.pdf
- New England Consortium of Metabolic Programs
  http://newenglandconsortium.org/for-families/other-metabolic-disorders/organic-acid-disorders/msud/
- Orphanet: Classic maple syrup urine disease
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=268145
- Orphanet: Intermediate maple syrup urine disease
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=268162
- Orphanet: Maple syrup urine disease
  https://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
  https://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
  https://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

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  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20301495

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