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My46 Trait Profile

Maple syrup urine disease

Other Names: Branched-Chain Ketoacid Dehydrogenase Deficiency

Maple Syrup Urine Disease is a metabolic disorder characterized by the body's inability to fully break down certain branched chain amino acids called leucine, isoleucine and valine. It is caused by mutations in the BCKDHA, BCKDHB, and DBT genes that make the branched chain ketoacid dehydrogenase enzyme complex.

Characteristics of Maple syrup urine disease

Individuals with Maple Syrup Urine Disease (MSUD) cannot break down certain branched chain amino acids call leucine, isoleucine and valine. Amino acids are the building blocks of protein. These three amino acids cannot be broken down because the enzyme complex, branched chain ketoacid dehydrogenase (BCKAD) is not working properly. The disease got its name because the urine of affected individuals may smell like maple sugar or burnt sugar. Babies who have MSUD are usually normal at birth, but they may be at risk for a metabolic crisis. A metabolic crisis is a serious health condition caused by the build-up of harmful substances in the blood. Symptoms of a metabolic crisis are poor feeding, vomiting, lethargy, excessive sleepiness and irritability. If a metabolic crisis is not treated, breathing problems, seizures, coma, and sometimes death can occur. Rarely, there are milder variants of MSUD which can lead to poor weight gain, poor growth, irritability or developmental delays later in infancy or childhood.

Diagnosis/Testing

Most infants with MSUD are diagnosed within the first few days or weeks of life through newborn screening (NBS). NBS tests a spot of blood from the baby's heel to see if the BCKAD enzyme complex is working properly. NBS test results are confirmed with additional blood and urine chemical tests, and possibly with genetic testing of the 3 BCKAD genes. These genes work together to make the branched chain ketoacid dehydrogenase enzyme complex that is responsible for breaking down or processing leucine, isoleucine and valine. Forty-five percent of individuals with MSUD have changes or mutations in both copies of one of the BCKDHA gene, 35% of individuals with MSUD have mutations in the BCKDHB (35%), and 20% of individuals with MSUD have mutations in the DBT (20%) gene.

Management/Surveillance

Since the amino acids leucine, isoleucine, and valine are found in most foods we eat, including breast milk and infant formula, it is very important that individuals with MSUD follow a special low protein diet. This diet includes a special medical formula and medical foods that provides nutrition to grow, but does not contain the branched chain amino acids (leucine, isoleucine, and valine). Frequent clinical and blood monitoring is often required, therefore children with MSUD should be managed by a team of specialists. It is recommended that an emergency treatment plan is made to ensure that during times of illness, a child with MSUD will be assessed for signs and symptoms of a metabolic crisis (e.g., poor feeding, vomiting, lethargy, excessive sleepiness, irritability) and treated appropriately. Rarely some individuals with MSUD are treated using a liver transplant.

Mode of inheritance

MSUD is inherited in an autosomal recessive pattern. This means that an individual has to inherit two mutations

(i.e., one from each parent) to be affected with MSUD. If both parents are carriers of mutations in the same gene, they have a 1 in 4 (25%) chance with each pregnancy of having a child with MSUD. Babies born in the United States are screened for MSUD by newborn screening.

Risk to family members

Parents of a child with MSUD are carriers for the condition. If a sibling of a child with MSUD is unaffected, he/she has a 2 in 3 (66%) chance of being a carrier of MSUD.

Special considerations

None

Resources

Genetics Home Reference: Maple Syrup Urine Disease
http://ghr.nlm.nih.gov/condition/maple-syrup-urine-disease
Medical Home Portal: Maple Syrup Urine Disease
http://www.medicalhomeportal.org/newborn/maple-syrup-urine-disease
Maple Syrup Urine Disease Family Support Group
http://www.msud-support.org/

References

Morton DH. et al. (2002)."Diagnosis and treatment of maple syrup disease: a study of 36 patients." Pediatrics 109(6): 999-1008.
Strauss, KA. et al. (Updated 9 May 2013). Maple Syrup Urine Disease. In: GeneReviews at GeneTests Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2013. Available at http://www.ncbi.nlm.nih.gov/books/NBK1319/ Accessed [01/14/2014].

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