Maple Syrup Urine Disease Type 1A (BCKDHA)

Maple syrup urine disease (MSUD) can be caused by mutations in a number of different genes, such as the BCKDHA gene. The BCKDHA gene encodes for the alpha subunit of the enzyme complex known as branched-chain alpha-keto acid dehydrogenase (BCKD), which is essential for the breakdown of branched chain amino-acids (leucine, isoleucine, and valine). Maple syrup urine disease is named due the sweet “maple syrup” smell from the urine of those with the disease. In the most common form of MSUD, untreated babies suffer from poor feeding and vomiting, followed by poor breathing, lethargy, and seizures. Death normally occurs within a few weeks of birth. Treatment is possible using special formula milk, followed by a special diet as an infant becomes older. However, it is difficult to always balance the amount of branched chain amino acids in the diet, since a small amounts must be supplied to maintain health. As they grow up, those with the condition tend to suffer from movement disorders, such as tremors, and various mental problems such as ADHD, low intelligence, autism, depression, and anxiety. In a minority of cases, the disease first shows itself later in infancy or during childhood, rather than immediately after birth. Some children suffer from an intermittent form of MSUD, where they appear normal most of the time, but attacks of the disease can be triggered by infections, stress, etc. Both the common form of the disease and the less severe forms can occur with defects in the BCKDA (Type 1A), BCKDB (Type 1B), and DBT (Type 2) genes; there is not a simple relation between severity and which gene is the cause.

All types of Maple syrup urine disease occurs in about 1 in 185,000 live births worldwide. However, it is much more prevalent in old order Amish (BCKDHA defects) and Ashkenazi Jewish families (BCKDHB defects). The frequency of the disease reaches 1 in 380 live births in some old order Amish communities. The faulty gene is inherited in an autosomal recessive manner, typically requiring both parents to be asymptomatic carriers.

Sources

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