Biotinidase deficiency

Biotinidase deficiency is an inherited disorder in which the body is unable to recycle the vitamin biotin. If this condition is not recognized and treated, its signs and symptoms typically appear within the first few months of life, although it can also become apparent later in childhood.

Profound biotinidase deficiency, the more severe form of the condition, can cause seizures, weak muscle tone (hypotonia), breathing problems, hearing and vision loss, problems with movement and balance (ataxia), skin rashes, hair loss (alopecia), and a fungal infection called candidiasis. Affected children also have delayed development. Lifelong treatment can prevent these complications from occurring or improve them if they have already developed.

Partial biotinidase deficiency is a milder form of this condition. Without treatment, affected children may experience hypotonia, skin rashes, and hair loss, but these problems may appear only during illness, infection, or other times of stress.

Frequency

Profound or partial biotinidase deficiency occurs in approximately 1 in 60,000 newborns

Causes

Mutations in the *BTD* gene cause biotinidase deficiency. The *BTD* gene provides instructions for making an enzyme called biotinidase. This enzyme recycles biotin, a B vitamin found in foods such as liver, egg yolks, and milk. Biotinidase removes biotin that is bound to proteins in food, leaving the vitamin in its free (unbound) state. Free biotin is needed by enzymes called biotin-dependent carboxylases to break down fats, proteins, and carbohydrates. Because several of these enzymes are impaired in biotinidase deficiency, the condition is considered a form of multiple carboxylase deficiency.

Mutations in the *BTD* gene reduce or eliminate the activity of biotinidase. Profound biotinidase deficiency results when the activity of biotinidase is reduced to less than 10 percent of normal. Partial biotinidase deficiency occurs when biotinidase activity is reduced to between 10 percent and 30 percent of normal. Without enough of this enzyme, biotin cannot be recycled. The resulting shortage of free biotin impairs the activity of biotin-dependent carboxylases, leading to a buildup of potentially toxic compounds in the body. If the condition is not treated promptly, this buildup damages various cells and tissues, causing the signs and symptoms described above.

Inheritance Pattern

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

biotinidase deficiency each carry one copy of the mutated gene, but they typically do not have any health problems associated with the condition.

Other Names for This Condition

- BIOT
- BTD deficiency
- carboxylase deficiency, multiple, late-onset
- late-onset biotin-responsive multiple carboxylase deficiency
- late-onset multiple carboxylase deficiency
- multiple carboxylase deficiency, late-onset

Diagnosis & Management

Formal Diagnostic Criteria

- ACT Sheet: Absent/Reduced biotinidase activity
  https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/Biotinidase.pdf

Genetic Testing Information

- What is genetic testing?
  /primer/testing/genetictesting
- Genetic Testing Registry: Biotinidase deficiency
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0220754/

Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22biotinidase+deficiency%22

Other Diagnosis and Management Resources

- Baby's First Test
  https://www.babysfirsttest.org/newborn-screening/conditions/biotinidase-deficiency
- GeneReview: Biotinidase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1322
- MedlinePlus Encyclopedia: Pantothenic Acid and Biotin
  https://medlineplus.gov/ency/article/002410.htm

Additional Information & Resources

Health Information from MedlinePlus

- Encyclopedia: Pantothenic Acid and Biotin
  https://medlineplus.gov/ency/article/002410.htm
- Health Topic: Genetic Brain Disorders
  https://medlineplus.gov/geneticbraindisorders.html
- Health Topic: Metabolic Disorders
  https://medlineplus.gov/metabolicdisorders.html
- Health Topic: Newborn Screening
  https://medlineplus.gov/newbornscreening.html

Genetic and Rare Diseases Information Center

- Biotinidase deficiency
  https://rarediseases.info.nih.gov/diseases/894/biotinidase-deficiency

Educational Resources

- Illinois Department of Public Health Newborn Screening Program
  http://www.idph.state.il.us/HealthWellness/fs/biotinidase.htm
- MalaCards: biotinidase deficiency
  https://www.malacards.org/card/biotinidase_deficiency
- Orphanet: Multiple carboxylase deficiency
  https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=148
- Virginia Department of Health
  http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_BIOT_English.pdf

Patient Support and Advocacy Resources

- Biotinidase Deficiency Family Support Group
  http://biotinidasedeficiency.20m.com/
- Metabolic Support UK
  https://www.metabolicsupportuk.org/
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/biotinidase-deficiency/

Clinical Information from GeneReviews

- Biotinidase Deficiency
  https://www.ncbi.nlm.nih.gov/books/NBK1322

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28biotinidase+deficiency%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- BIOTINIDASE DEFICIENCY
  http://omim.org/entry/253260

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