



## 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

### Genetic Changes

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

- Genetic Testing Registry: Biotinidase deficiency  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0220754/>

### Other Diagnosis and Management Resources

- Baby's First Test  
<http://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>

### 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: 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

- Children Living With Inherited Metabolic Diseases (CLIMB) (UK): Biotinidase Deficiency  
<http://www.climb.org.uk/IMD/Bravo/BiotinidaseDeficiency.pdf>
- Disease InfoSearch: Biotinidase Deficiency  
<http://www.diseaseinfosearch.org/Biotinidase+Deficiency/846>
- Illinois Department of Public Health Newborn Screening Program  
<http://www.idph.state.il.us/HealthWellness/fs/biotinidase.htm>
- MalaCards: biotinidase deficiency  
[http://www.malacards.org/card/biotinidase\\_deficiency](http://www.malacards.org/card/biotinidase_deficiency)
- My46 Trait Profile  
<https://www.my46.org/trait-document?trait=Biotinidase%20deficiency&type=profile>

- Orphanet: Multiple carboxylase deficiency  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=148](http://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](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/>
- Children Living with Inherited Metabolic Diseases (CLIMB) (UK)  
<http://www.climb.org.uk/>
- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/biotinidase-deficiency/>

#### GeneReviews

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

#### ClinicalTrials.gov

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

#### 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>

#### OMIM

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

#### **Sources for This Summary**

- Dobrowolski SF, Angeletti J, Banas RA, Naylor EW. Real time PCR assays to detect common mutations in the biotinidase gene and application of mutational analysis to newborn screening for biotinidase deficiency. *Mol Genet Metab.* 2003 Feb;78(2):100-7.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/12618081>
- Sivri HS, Genç GA, Tokatli A, Dursun A, Coskun T, Aydin HI, Sennaroglu L, Belgin E, Jensen K, Wolf B. Hearing loss in biotinidase deficiency: genotype-phenotype correlation. *J Pediatr.* 2007 Apr; 150(4):439-42. Erratum in: *J Pediatr.* 2007 Aug;151(2):222. Tokatly, Aysegül [corrected to Tokatli, Aysegül]; Aydyn, Halil Ybrahim [corrected to Aydin, Halil Ibrahim].  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/17382128>

- Wolf B. Biotinidase Deficiency. 2000 Mar 24 [updated 2016 Jun 9]. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. Available from <http://www.ncbi.nlm.nih.gov/books/NBK1322/>  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/20301497>
  - Wolf B. Biotinidase deficiency: "if you have to have an inherited metabolic disease, this is the one to have". *Genet Med*. 2012 Jun;14(6):565-75. doi: 10.1038/gim.2011.6. Epub 2012 Jan 5. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/22241090>
  - Wolf B. Clinical issues and frequent questions about biotinidase deficiency. *Mol Genet Metab*. 2010 May;100(1):6-13. doi: 10.1016/j.ymgme.2010.01.003. Epub 2010 Jan 11. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/20129807>
  - Wolf B. The neurology of biotinidase deficiency. *Mol Genet Metab*. 2011 Sep-Oct;104(1-2):27-34. doi: 10.1016/j.ymgme.2011.06.001. Epub 2011 Jun 12. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/21696988>
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