



## beta-ketothiolase deficiency

Beta-ketothiolase deficiency is an inherited disorder in which the body cannot effectively process a protein building block (amino acid) called isoleucine. This disorder also impairs the body's ability to process ketones, which are molecules produced during the breakdown of fats.

The signs and symptoms of beta-ketothiolase deficiency typically appear between the ages of 6 months and 24 months. Affected children experience episodes of vomiting, dehydration, difficulty breathing, extreme tiredness (lethargy), and, occasionally, seizures. These episodes, which are called ketoacidotic attacks, sometimes lead to coma. Ketoacidotic attacks are frequently triggered by infections, periods without food (fasting), or increased intake of protein-rich foods.

### Frequency

Beta-ketothiolase deficiency appears to be very rare. It is estimated to affect fewer than 1 in 1 million newborns.

### Genetic Changes

Mutations in the *ACAT1* gene cause beta-ketothiolase deficiency. This gene provides instructions for making an enzyme that is found in the energy-producing centers within cells (mitochondria). This enzyme plays an essential role in breaking down proteins and fats from the diet. Specifically, the ACAT1 enzyme helps process isoleucine, which is a building block of many proteins, and ketones, which are produced during the breakdown of fats.

Mutations in the *ACAT1* gene reduce or eliminate the activity of the ACAT1 enzyme. A shortage of this enzyme prevents the body from processing proteins and fats properly. As a result, related compounds can build up to toxic levels in the blood. These substances cause the blood to become too acidic (ketoacidosis), which can damage the body's tissues and organs, particularly in the nervous system.

### 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

- 2-alpha-methyl-3-hydroxybutyricacidemia
- 3-alpha-ketothiolase deficiency
- 3-alpha-ktd deficiency
- 3-alpha-oxothiolase deficiency
- 3-Ketothiolase deficiency
- 3-Methylhydroxybutyric acidemia
- alpha-Methylacetoacetic aciduria
- BKT
- MAT deficiency
- Mitochondrial 2-methylacetoacetyl-CoA thiolase deficiency - potassium stimulated
- Mitochondrial acetoacetyl-CoA thiolase deficiency
- T2 deficiency
- $\beta$ -ketothiolase deficiency

## Diagnosis & Management

These resources address the diagnosis or management of beta-ketothiolase deficiency:

- Baby's First Test  
<http://www.babysfirsttest.org/newborn-screening/conditions/beta-ketothiolase-deficiency>
- Genetic Testing Registry: Deficiency of acetyl-CoA acetyltransferase  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1536500/>

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>

## **Additional Information & Resources**

### MedlinePlus

- 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

- Beta ketothiolase deficiency  
<https://rarediseases.info.nih.gov/diseases/872/beta-ketothiolase-deficiency>

### Educational Resources

- Disease InfoSearch: Beta Ketothiolase Deficiency  
<http://www.diseaseinfosearch.org/Beta+Ketothiolase+Deficiency/812>
- My46 Trait Profile  
<https://www.my46.org/trait-document?trait=Beta%20ketothiolase%20deficiency&type=profile>
- Orphanet: Beta-ketothiolase deficiency  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=134](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=134)
- Screening, Technology And Research in Genetics  
<http://www.newbornscreening.info/Parents/organicacididorders/BKD.html>
- Virginia Department of Health  
[http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet\\_BKT\\_English.pdf](http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_BKT_English.pdf)

### Patient Support and Advocacy Resources

- Children Living with Inherited Metabolic Diseases  
<http://www.climb.org.uk/>
- Organic Acidemia Association  
<http://www.oaanews.org/bkt.html>

## Genetic Testing Registry

- Deficiency of acetyl-CoA acetyltransferase  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1536500/>

## ACT Sheets

- Elevated C5-OH Acylcarnitine  
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C5-OH.pdf>

## Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28beta-ketothiolase+deficiency%5BTIAB%5D%29+OR+%283-ketothiolase+deficiency%5BTIAB%5D%29+OR+%28alpha-methylacetoacetic+aciduria%5BTIAB%5D%29+OR+%28peroxisomal+thiolase+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

## OMIM

- ALPHA-METHYLACETOACETIC ACIDURIA  
<http://omim.org/entry/203750>

## **Sources for This Summary**

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Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/beta-ketothiolase-deficiency>

Reviewed: January 2008

Published: February 14, 2017

Lister Hill National Center for Biomedical Communications

U.S. National Library of Medicine

National Institutes of Health

Department of Health & Human Services