



## 3-methylcrotonyl-CoA carboxylase deficiency

3-methylcrotonyl-CoA carboxylase deficiency (also known as 3-MCC deficiency) is an inherited disorder in which the body is unable to process certain proteins properly. People with this disorder have a shortage of an enzyme that helps break down proteins containing a particular building block (amino acid) called leucine.

Infants with 3-MCC deficiency appear normal at birth but usually develop signs and symptoms in infancy or early childhood. The characteristic features of this condition, which can range from mild to life-threatening, include feeding difficulties, recurrent episodes of vomiting and diarrhea, excessive tiredness (lethargy), and weak muscle tone (hypotonia). If untreated, this disorder can lead to delayed development, seizures, and coma. Many of these complications can be prevented with early detection and lifelong management with a low-protein diet and appropriate supplements. Some people with gene mutations that cause 3-MCC deficiency never experience any signs or symptoms of the condition.

The characteristic features of 3-MCC deficiency are similar to those of Reye syndrome, a severe disorder that develops in children while they appear to be recovering from viral infections such as chicken pox or flu. Most cases of Reye syndrome are associated with the use of aspirin during these viral infections.

### Frequency

This condition is detected in an estimated 1 in 36,000 newborns worldwide.

### Causes

Mutations in the *MCCC1* or *MCCC2* gene can cause 3-MCC deficiency. These two genes provide instructions for making different parts (subunits) of an enzyme called 3-methylcrotonyl-coenzyme A carboxylase (3-MCC). This enzyme plays a critical role in breaking down proteins obtained from the diet. Specifically, 3-MCC is responsible for the fourth step in processing leucine, an amino acid that is part of many proteins.

Mutations in the *MCCC1* or *MCCC2* gene reduce or eliminate the activity of 3-MCC, preventing the body from processing leucine properly. As a result, toxic byproducts of leucine processing build up to harmful levels, which can damage the brain. This damage underlies the signs and symptoms of 3-MCC deficiency.

### 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

- 3-MCC
- 3-MCC deficiency
- 3-methylcrotonyl-coenzyme A carboxylase deficiency
- 3-methylcrotonylglycinuria
- 3MCC
- BMCC deficiency
- Deficiency of methylcrotonoyl-CoA carboxylase
- MCC deficiency
- Methylcrotonyl-CoA carboxylase deficiency

## Diagnosis & Management

### Formal Treatment/Management Guidelines

- New England Consortium of Metabolic Programs: Acute Illness Protocol  
[https://newenglandconsortium.org/protocols/acute\\_illness/organic\\_acid\\_disorders/3-MCC-dehydrogenase-def.pdf](https://newenglandconsortium.org/protocols/acute_illness/organic_acid_disorders/3-MCC-dehydrogenase-def.pdf)

### Genetic Testing Information

- What is genetic testing?  
</primer/testing/genetic-testing>
- Genetic Testing Registry: 3-MCC Deficiency  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268600/>
- Genetic Testing Registry: 3 Methylcrotonyl-CoA carboxylase 1 deficiency  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/CN028786/>
- Genetic Testing Registry: 3-methylcrotonyl CoA carboxylase 2 deficiency  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1859499/>

### Other Diagnosis and Management Resources

- Baby's First Test  
<https://www.babysfirsttest.org/newborn-screening/conditions/3-methylcrotonyl-coa-carboxylase-deficiency>

## **Additional Information & Resources**

### Health Information from 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

- 3 Methylcrotonyl-CoA carboxylase 1 deficiency  
<https://rarediseases.info.nih.gov/diseases/5665/3-methylcrotonyl-coa-carboxylase-1-deficiency>
- 3-methylcrotonyl-CoA carboxylase deficiency  
<https://rarediseases.info.nih.gov/diseases/10954/3-methylcrotonyl-coa-carboxylase-deficiency>

### Educational Resources

- MalaCards: 3-methylcrotonyl-coa carboxylase 1 deficiency  
[https://www.malacards.org/card/3\\_methylcrotonyl\\_coa\\_carboxylase\\_1\\_deficiency\\_2](https://www.malacards.org/card/3_methylcrotonyl_coa_carboxylase_1_deficiency_2)
- MalaCards: 3-methylcrotonyl-coa carboxylase 2 deficiency  
[https://www.malacards.org/card/3\\_methylcrotonyl\\_coa\\_carboxylase\\_2\\_deficiency](https://www.malacards.org/card/3_methylcrotonyl_coa_carboxylase_2_deficiency)
- MalaCards: 3-methylcrotonyl-coa carboxylase deficiency  
[https://www.malacards.org/card/3\\_methylcrotonyl\\_coa\\_carboxylase\\_deficiency](https://www.malacards.org/card/3_methylcrotonyl_coa_carboxylase_deficiency)
- Newborn Screening Ontario (Canada): C5OH-related Targets  
<https://www.newbornscreening.on.ca/en/c5oh-related-targets>
- Orphanet: 3-methylcrotonyl-CoA carboxylase deficiency  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=6](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=6)
- Screening, Technology, and Research in Genetics  
<http://www.newbornscreening.info/Parents/organicacid disorders/3MCC.html>
- Virginia Department of Health  
[http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet\\_3MCC\\_English.pdf](http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_3MCC_English.pdf)

### Patient Support and Advocacy Resources

- Metabolic Support (UK)  
<https://www.metabolicsupportuk.org/>
- Organic Acidemia Association  
<https://www.oaanews.org/3-mcc.html>
- Resource list from the University of Kansas Medical Center  
<http://www.kumc.edu/gec/support/organic.html>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%283-methylcrotonyl-coa+carboxylase+deficiency%5BTIAB%5D%29+OR+%283-mcc%5BTIAB%5D%29+OR+%28mcc+deficiency%5BTIAB%5D%29+OR+%28methylcrotonyl-coa+carboxylase+deficiency%5BTIAB%5D%29+OR+%283-methylcrotonylglycinuria%5BTIAB%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

### Catalog of Genes and Diseases from OMIM

- 3-METHYLCROTONYL-CoA CARBOXYLASE 1 DEFICIENCY  
<http://omim.org/entry/210200>
- 3-METHYLCROTONYL-CoA CARBOXYLASE 2 DEFICIENCY  
<http://omim.org/entry/210210>

### Medical Genetics Database from MedGen

- 3-MCC Deficiency  
<https://www.ncbi.nlm.nih.gov/medgen/78691>
- 3 Methylcrotonyl-CoA carboxylase 1 deficiency  
<https://www.ncbi.nlm.nih.gov/medgen/468532>
- 3-methylcrotonyl CoA carboxylase 2 deficiency  
<https://www.ncbi.nlm.nih.gov/medgen/347898>

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