



## Mitochondrial trifunctional protein deficiency

Mitochondrial trifunctional protein deficiency is a rare condition that prevents the body from converting certain fats to energy, particularly during periods without food (fasting).

Signs and symptoms of mitochondrial trifunctional protein deficiency may begin during infancy or later in life. Features that occur during infancy include feeding difficulties, lack of energy (lethargy), low blood sugar (hypoglycemia), weak muscle tone (hypotonia), and liver problems. Infants with this disorder are also at high risk for serious heart problems, breathing difficulties, coma, and sudden death. Signs and symptoms of mitochondrial trifunctional protein deficiency that may begin after infancy include hypotonia, muscle pain, a breakdown of muscle tissue, and a loss of sensation in the extremities (peripheral neuropathy).

Problems related to mitochondrial trifunctional protein deficiency can be triggered by periods of fasting or by illnesses such as viral infections. This disorder is sometimes mistaken for Reye syndrome, a severe disorder that may develop 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

Mitochondrial trifunctional protein deficiency is a rare disorder; its incidence is unknown.

### Causes

Mutations in the *HADHA* and *HADHB* genes cause mitochondrial trifunctional protein deficiency. These genes each provide instructions for making part of an enzyme complex called mitochondrial trifunctional protein. This enzyme complex functions in mitochondria, the energy-producing centers within cells. As the name suggests, mitochondrial trifunctional protein contains three enzymes that each perform a different function. This enzyme complex is required to break down (metabolize) a group of fats called long-chain fatty acids. Long-chain fatty acids are found in foods such as milk and certain oils. These fatty acids are stored in the body's fat tissues. Fatty acids are a major source of energy for the heart and muscles. During periods of fasting, fatty acids are also an important energy source for the liver and other tissues.

Mutations in the *HADHA* or *HADHB* genes that cause mitochondrial trifunctional protein deficiency disrupt all three functions of this enzyme complex. Without enough of this enzyme complex, long-chain fatty acids from food and body fat cannot be metabolized and processed. As a result, these fatty acids are not converted to energy, which can lead to some features of this disorder, such as lethargy and hypoglycemia. Long-chain fatty acids or partially metabolized fatty acids may also build up and damage the liver,

heart, and muscles. This abnormal buildup causes the other signs and symptoms of mitochondrial trifunctional protein 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**

- MTP deficiency
- TFP deficiency
- TPA deficiency
- trifunctional protein deficiency, type 2

### **Diagnosis & Management**

#### Formal Diagnostic Criteria

- ACT Sheet: Elevated C16-OH +/- C18:1-OH and Other Long Chain Acylcarnitines  
<https://www.ncbi.nlm.nih.gov/books/NBK55827/bin/C16-OH.pdf>

#### Genetic Testing Information

- What is genetic testing?  
</primer/testing/genetic-testing>
- Genetic Testing Registry: Mitochondrial trifunctional protein deficiency  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C1969443/>

#### Research Studies from ClinicalTrials.gov

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

#### Other Diagnosis and Management Resources

- Baby's First Test  
<https://www.babysfirsttest.org/newborn-screening/conditions/trifunctional-protein-deficiency>
- MedlinePlus Encyclopedia: Hypoglycemia  
<https://medlineplus.gov/ency/article/000386.htm>
- MedlinePlus Encyclopedia: Peripheral Neuropathy  
<https://medlineplus.gov/ency/article/000593.htm>

## **Additional Information & Resources**

### Health Information from MedlinePlus

- Encyclopedia: Hypoglycemia  
<https://medlineplus.gov/ency/article/000386.htm>
- Encyclopedia: Peripheral Neuropathy  
<https://medlineplus.gov/ency/article/000593.htm>
- Health Topic: Mitochondrial Diseases  
<https://medlineplus.gov/mitochondrialdiseases.html>
- Health Topic: Newborn Screening  
<https://medlineplus.gov/newbornscreening.html>

### Genetic and Rare Diseases Information Center

- Mitochondrial trifunctional protein deficiency  
<https://rarediseases.info.nih.gov/diseases/3684/mitochondrial-trifunctional-protein-deficiency>

### Educational Resources

- Illinois Department of Public Health  
<http://www.idph.state.il.us/HealthWellness/fs/mcad.htm>
- MalaCards: mitochondrial trifunctional protein deficiency  
[https://www.malacards.org/card/mitochondrial\\_trifunctional\\_protein\\_deficiency](https://www.malacards.org/card/mitochondrial_trifunctional_protein_deficiency)
- Orphanet: Mitochondrial trifunctional protein deficiency  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=746](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=746)
- Screening, Technology, and Research in Genetics  
<http://www.newbornscreening.info/Parents/fattyaciddisorders/TFP.html>
- Virginia Department of Health  
[http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet\\_TFP\\_English.pdf](http://www.vdh.virginia.gov/content/uploads/sites/33/2016/11/Parent-Fact-Sheet_TFP_English.pdf)

### Patient Support and Advocacy Resources

- Children's Mitochondrial Disease Network (UK)  
<http://www.cmdn.org.uk/>
- FOD (Fatty Oxidation Disorders) Family Support Group  
<https://fodsupport.org/>
- Metabolic Support UK  
<https://www.metabolicsupportuk.org/>
- United Mitochondrial Disease Foundation  
<https://www.umdf.org/>

## Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28mitochondrial+trifunctional+protein+deficiency%5BTIAB%5D%29+OR+%28TFP+deficiency%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

## Catalog of Genes and Diseases from OMIM

- MITOCHONDRIAL TRIFUNCTIONAL PROTEIN DEFICIENCY  
<http://omim.org/entry/609015>

## Medical Genetics Database from MedGen

- Trifunctional Protein Deficiency, Type 2  
<https://www.ncbi.nlm.nih.gov/medgen/780845>

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