



## Ornithine transcarbamylase deficiency

Ornithine transcarbamylase deficiency is an inherited disorder that causes ammonia to accumulate in the blood. Ammonia, which is formed when proteins are broken down in the body, is toxic if the levels become too high. The nervous system is especially sensitive to the effects of excess ammonia.

Ornithine transcarbamylase deficiency can become evident at any age. The most severe form occurs in the first few days of life. This neonatal-onset form of the disorder usually affects males; it is very rare in females. An infant with the neonatal-onset form of ornithine transcarbamylase deficiency may be lacking in energy (lethargic) or unwilling to eat, and have a poorly-controlled breathing rate or body temperature. Infants with this disorder may be described as "floppy" and can experience seizures or coma. Complications from ornithine transcarbamylase deficiency may include developmental delay and intellectual disability. Progressive liver damage may also occur.

In some affected individuals, signs and symptoms of ornithine transcarbamylase deficiency may be less severe, and may not appear until later in life. The late-onset form of the disorder occurs in both males and females. People with late-onset ornithine transcarbamylase deficiency may experience episodes of altered mental status, such as delirium, erratic behavior, or a reduced level of consciousness. Headaches, vomiting, aversion to protein foods, and seizures can also occur in this form of the disorder.

### Frequency

Estimates of the prevalence of ornithine transcarbamylase deficiency have ranged from 1 in 14,000 to 1 in 77,000 people. Individuals with the neonatal-onset form of the disorder are more likely to be counted in these estimates, because people with the late-onset form are less likely to come to medical attention.

### Causes

Mutations in the *OTC* gene cause ornithine transcarbamylase deficiency. The *OTC* gene provides instructions for making the ornithine transcarbamylase enzyme.

Ornithine transcarbamylase deficiency belongs to a class of genetic diseases called urea cycle disorders. The urea cycle is a sequence of reactions that occurs in liver cells. It processes excess nitrogen, generated when protein is used by the body, to make a compound called urea that is excreted by the kidneys. The ornithine transcarbamylase enzyme starts a specific reaction within the urea cycle.

In ornithine transcarbamylase deficiency, as its name suggests, the ornithine transcarbamylase enzyme is damaged or missing. The urea cycle cannot proceed normally, and nitrogen accumulates in the bloodstream in the form of ammonia.

Ammonia is especially damaging to the nervous system, so ornithine transcarbamylase deficiency causes neurological problems as well as eventual damage to the liver.

### **Inheritance Pattern**

Ornithine transcarbamylase deficiency is an X-linked disorder. A condition is considered X-linked if the mutated gene that causes the disorder is located on the X chromosome, one of the two sex chromosomes. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In males (who have only one X chromosome), one altered copy of the gene in each cell is sufficient to cause the condition. In females (who have two X chromosomes), mutations in both copies of the gene will cause the disorder. Some females with only one altered copy of the *OTC* gene also show signs and symptoms of ornithine transcarbamylase deficiency.

### **Other Names for This Condition**

- Ornithine Carbamoyltransferase Deficiency Disease

### **Diagnosis & Management**

#### Formal Treatment/Management Guidelines

- New England Consortium of Metabolic Programs: Acute Illness Protocol  
<http://newenglandconsortium.org/for-professionals/acute-illness-protocols/urea-cycle-disorders/ornithine-transcarbamylase-deficiency-otc/>

#### Genetic Testing Information

- What is genetic testing?  
</primer/testing/genetic-testing>
- Genetic Testing Registry: Ornithine carbamoyltransferase deficiency  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0268542/>

#### Research Studies from ClinicalTrials.gov

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

### Other Diagnosis and Management Resources

- Baby's First Test  
<https://www.babysfirsttest.org/newborn-screening/conditions/ornithine-transcarbamylase-deficiency>
- GeneReview: Ornithine Transcarbamylase Deficiency  
<https://www.ncbi.nlm.nih.gov/books/NBK154378>
- GeneReview: Urea Cycle Disorders Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK1217>
- MedlinePlus Encyclopedia: Hereditary urea cycle abnormality  
<https://medlineplus.gov/ency/article/000372.htm>
- National Organization for Rare Disorders (NORD) Physician Guide: Urea Cycle Disorders  
<https://rarediseases.org/physician-guide/urea-cycle-disorders/>

### **Additional Information & Resources**

#### Health Information from MedlinePlus

- Encyclopedia: Hereditary urea cycle abnormality  
<https://medlineplus.gov/ency/article/000372.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

- Ornithine transcarbamylase deficiency  
<https://rarediseases.info.nih.gov/diseases/8391/ornithine-transcarbamylase-deficiency>

#### Educational Resources

- MalaCards: ornithine transcarbamylase deficiency, hyperammonemia due to  
[https://www.malacards.org/card/ornithine\\_transcarbamylase\\_deficiency\\_hyperammonemia\\_due\\_to](https://www.malacards.org/card/ornithine_transcarbamylase_deficiency_hyperammonemia_due_to)
- Orphanet: Ornithine transcarbamylase deficiency  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=664](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=664)

### Patient Support and Advocacy Resources

- Metabolic Support UK  
<https://www.metabolicsupportuk.org/>
- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/ornithine-transcarbamylase-deficiency/>
- National Urea Cycle Disorders Foundation  
<http://nucdf.org>
- Urea Cycle Disorders Consortium  
<https://www.rarediseasesnetwork.org/cms/UCDC>

### Clinical Information from GeneReviews

- Ornithine Transcarbamylase Deficiency  
<https://www.ncbi.nlm.nih.gov/books/NBK154378>
- Urea Cycle Disorders Overview  
<https://www.ncbi.nlm.nih.gov/books/NBK1217>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28Ornithine+Carbamoyltransferase+Deficiency+Disease%5BMAJR%5D%29+AND+%28ornithine+transcarbamylase+deficiency%5BTIAB%5D%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

### Catalog of Genes and Diseases from OMIM

- ORNITHINE TRANSCARBAMYLASE DEFICIENCY, HYPERAMMONEMIA DUE TO  
<http://omim.org/entry/311250>

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