

## DOORS syndrome

### Description

DOORS syndrome is a disorder involving multiple abnormalities that are present from birth (congenital). "DOORS" is an abbreviation for the major features of the disorder including deafness; short or absent nails (onychodystrophy); short fingers and toes (osteodystrophy); developmental delay and intellectual disability (previously called mental retardation); and seizures. Some people with DOORS syndrome do not have all of these features.

Most people with DOORS syndrome have profound hearing loss caused by changes in the inner ears (sensorineural deafness). Developmental delay and intellectual disability are also often severe in this disorder.

The nail abnormalities affect both the hands and the feet in DOORS syndrome. Impaired growth of the bones at the tips of the fingers and toes (hypoplastic terminal phalanges) account for the short fingers and toes characteristic of this disorder. Some affected individuals also have an extra bone and joint in their thumbs, causing the thumbs to look more like the other fingers (triphalangeal thumbs).

The seizures that occur in people with DOORS syndrome usually start in infancy. The most common seizures in people with this condition are generalized tonic-clonic seizures (also known as grand mal seizures), which cause muscle rigidity, convulsions, and loss of consciousness. Affected individuals may also have other types of seizures, including partial seizures, which affect only one area of the brain and do not cause a loss of consciousness; absence seizures, which cause loss of consciousness for a short period that appears as a staring spell; or myoclonic seizures, which cause rapid, uncontrolled muscle jerks. In some affected individuals the seizures increase in frequency and become more severe and difficult to control, and a potentially life-threatening prolonged seizure (status epilepticus) can occur.

Other features that can occur in people with DOORS syndrome include an unusually small head size (microcephaly) and facial differences, most commonly a wide, bulbous nose. A narrow or high arched roof of the mouth (palate), broadening of the ridges in the upper and lower jaw that contain the sockets of the teeth (alveolar ridges), or shortening of the membrane between the floor of the mouth and the tongue (frenulum) have also been observed in some affected individuals. People with DOORS syndrome may also have dental abnormalities, structural abnormalities of the heart or urinary tract, and abnormally low levels of thyroid hormones (hypothyroidism). Most affected individuals

also have higher-than-normal levels of a substance called 2-oxoglutaric acid in their urine; these levels can fluctuate between normal and elevated.

## Frequency

DOORS syndrome is a rare disorder; its prevalence is unknown. Approximately 50 affected individuals have been described in the medical literature.

## Causes

DOORS syndrome can be caused by mutations in the *TBC1D24* gene. This gene provides instructions for making a protein whose specific function in the cell is unclear. Studies suggest the protein may have several roles in cells. The TBC1D24 protein belongs to a group of proteins that are involved in the movement (transport) of vesicles, which are small sac-like structures that transport proteins and other materials within cells. Research suggests that the TBC1D24 protein may also help cells respond to oxidative stress. Oxidative stress occurs when unstable molecules called free radicals accumulate to levels that can damage or kill cells. Studies indicate that the TBC1D24 protein is active in a variety of organs and tissues; it is particularly active in the brain and likely plays an important role in normal brain development. The TBC1D24 protein is also active in specialized structures called stereocilia. In the inner ear, stereocilia project from certain cells called hair cells. The stereocilia bend in response to sound waves, which is critical for converting sound waves to nerve impulses.

*TBC1D24* gene mutations that cause DOORS syndrome are thought to reduce or eliminate the function of the TBC1D24 protein, but the specific mechanism by which loss of TBC1D24 function leads to the signs and symptoms of DOORS syndrome is not well understood.

In about half of affected individuals, no *TBC1D24* gene mutation has been identified. The cause of DOORS syndrome in these individuals is unknown.

[Learn more about the gene associated with DOORS syndrome](#)

- TBC1D24

## Inheritance

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

- Autosomal recessive deafness-onychodystrophy syndrome
- Deafness, onychodystrophy, osteodystrophy, and mental retardation syndrome

- Deafness-onychodystrophy-osteodystrophy-intellectual disability syndrome
- Deafness-onychoosteodystrophy-intellectual disability syndrome
- Digitorenocerebral syndrome
- DOOR syndrome
- DRC syndrome
- Eronen syndrome

## **Additional Information & Resources**

### Genetic and Rare Diseases Information Center

- DOORS syndrome (<https://rarediseases.info.nih.gov/diseases/1685/index>)

### Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (<https://rarediseases.org/>)

### Catalog of Genes and Diseases from OMIM

- DEAFNESS, ONYCHODYSTROPHY, OSTEODYSTROPHY, IMPAIRED INTELLECTUAL DEVELOPMENT, AND SEIZURES SYNDROME; DOORS (<https://omim.org/entry/220500>)

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28DOORS+syndrome%5BTIAB%5D%29+OR+%28DOOR+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D>)

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**Last updated February 1, 2019**