

Norrie disease

Description

Norrie disease is an inherited eye disorder that leads to blindness in male infants at birth or soon after birth. It causes abnormal development of the retina, the layer of sensory cells that detect light and color, with masses of immature retinal cells accumulating at the back of the eye. As a result, the pupils appear white when light is shone on them, a sign called leukocoria. The irises (colored portions of the eyes) or the entire eyeballs may shrink and deteriorate during the first months of life, and cataracts (cloudiness in the lens of the eye) may eventually develop.

About 30 percent of individuals with Norrie disease develop progressive hearing loss, and 30 to 50 percent of people affected experience developmental delays in motor skills such as sitting up and walking. Other problems may include mild to moderate intellectual disability, often with psychosis, and abnormalities that can affect circulation, breathing, digestion, excretion, or reproduction.

Frequency

Norrie disease is a rare disorder; more than 400 cases have been reported in the scientific literature.

Causes

Mutations in the *NDP* gene cause Norrie disease. The *NDP* gene provides instructions for making a protein called norrin. Norrin participates in the Wnt cascade, a sequence of steps that affect the way cells and tissues develop. In particular, norrin seems to play a critical role in the specialization of retinal cells for their unique sensory capabilities. It is also involved in the establishment of a blood supply to tissues of the retina and the inner ear, and the development of other body systems.

In order to initiate the Wnt cascade, norrin must bind (attach) to another protein called frizzled-4. Mutations in the norrin protein interfere with its ability to bind to frizzled-4, resulting in the signs and symptoms of Norrie disease.

[Learn more about the gene associated with Norrie disease](#)

- NDP

Inheritance

This condition is inherited in an X-linked recessive pattern. 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. 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), a mutation must be present in both copies of the gene to cause the disorder. Males are affected by X-linked recessive disorders much more frequently than females. A characteristic of X-linked inheritance is that fathers cannot pass X-linked traits to their sons.

In X-linked recessive inheritance, a female with one altered copy of the gene in each cell is called a carrier. She can pass on the gene, but generally does not experience signs and symptoms of the disorder.

In rare cases, however, carrier females have shown some retinal abnormalities or mild hearing loss associated with Norrie disease. Females with one *NDP* gene mutation who show features of Norrie disease do so because of a process called X-inactivation. Early in embryonic development in females, one of the two X chromosomes is permanently turned off (inactivated) in somatic cells (cells other than egg and sperm cells). X-inactivation ensures that females, like males, have only one active copy of the X chromosome in each body cell. Usually X-inactivation occurs randomly, so that each X chromosome is active in about half the body's cells. This means that in females with an *NDP* gene mutation, the X chromosome with an *NDP* gene mutation is active in about half of cells, and the X chromosome with the normal *NDP* gene is active in about half. Because X-inactivation leads to some cells that produce functional norrin protein and some cells that do not, females can have some features of Norrie disease.

Other Names for This Condition

- Anderson-Warburg syndrome
- Atrophia bulborum hereditaria
- Congenital progressive oculo-acoustico-cerebral degeneration
- Episkopi blindness
- Fetal iritis syndrome
- Norrie syndrome
- Norrie's disease
- Norrie-Warburg syndrome
- Oligophrenia microphthalmus
- Pseudoglioma congenita
- Whitnall-Norman syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Atrophia bulborum hereditaria (<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0266526/>)

Genetic and Rare Diseases Information Center

- Norrie disease (<https://rarediseases.info.nih.gov/diseases/7224/index>)

Patient Support and Advocacy Resources

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

Clinical Trials

- ClinicalTrials.gov ([https://clinicaltrials.gov/search?cond=%22Norrie disease%22](https://clinicaltrials.gov/search?cond=%22Norrie+disease%22))

Catalog of Genes and Diseases from OMIM

- NORRIE DISEASE; ND (<https://omim.org/entry/310600>)

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28norrie+disease%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>)

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