



## Gillespie syndrome

Gillespie syndrome is a disorder that involves eye abnormalities, weak muscle tone from birth (congenital hypotonia), problems with balance and coordinating movements (ataxia), and mild to moderate intellectual disability.

Gillespie syndrome is characterized by underdevelopment (hypoplasia) of the colored part of the eye (the iris). In most affected individuals, part of the iris is missing (partial aniridia) in both eyes. In addition, the irises have a characteristic uneven pattern known as "scalloping" at the inner (pupillary) edge. The pupils are enlarged (dilated) and are fixed, which means they do not get smaller (constrict) in response to light. These abnormalities are thought to result from problems in the development or maintenance of the tiny muscles that allow the pupil to contract (sphincter pupillae). The eye abnormalities can cause blurry vision (reduced visual acuity) and increased sensitivity to light (photophobia). Rapid, involuntary eye movements (nystagmus) can also occur in Gillespie syndrome.

The balance and movement problems in Gillespie syndrome result from hypoplasia of the cerebellum, which is the part of the brain that coordinates movement. This abnormality can cause hypotonia and delayed development of motor skills such as walking. In addition, difficulty controlling the muscles of the mouth can lead to delayed speech development. The difficulties with coordination generally become noticeable in early childhood when the individual is learning these skills. People with Gillespie syndrome usually continue to have an unsteady pattern of walking (gait) and speech problems throughout life.

Other features of Gillespie syndrome can include abnormalities in the bones of the spine (vertebrae) and malformations of the heart.

### Frequency

The prevalence of Gillespie syndrome is unknown. Only a few dozen affected individuals have been described in the medical literature. It has been estimated that Gillespie syndrome accounts for about 2 percent of cases of aniridia.

### Causes

Gillespie syndrome is caused by mutations in the *ITPR1* gene. This gene provides instructions for making a protein that is part of a channel that controls the flow of positively charged calcium atoms (calcium ions) within cells. Four ITPR1 protein molecules join together in a complex (a homotetramer) to form the channel.

In response to certain signals, the ITPR1 channel releases calcium ions from storage in a cell structure called the endoplasmic reticulum into the surrounding cell fluid (the

cytoplasm). Proper regulation of calcium ion concentration inside cells is important for the development and function of various tissues and organs.

*ITPR1* gene mutations likely result in a protein that cannot form stable calcium channels. A shortage of ITPR1 channels impairs the cell's ability to regulate the concentration of calcium ions. However, the specific connection between these changes and the signs and symptoms of Gillespie syndrome is unclear.

## **Inheritance Pattern**

Gillespie syndrome can be inherited in an autosomal recessive pattern, which means both copies of a 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.

In some cases of Gillespie syndrome, the condition occurs in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. Some affected individuals inherit the mutation from one affected parent. Other cases result from new mutations in the gene and occur in people with no history of the disorder in their family. Autosomal dominant cases of Gillespie syndrome are thought to arise from a dominant-negative effect, which means that the altered protein produced from one copy of the gene interferes with the function of the normal protein produced from the other copy of the gene.

## **Other Names for This Condition**

- aniridia-cerebellar ataxia-intellectual disability
- aniridia-cerebellar ataxia-mental deficiency
- aniridia, cerebellar ataxia, and mental retardation
- partial aniridia-cerebellar ataxia-oligophrenia

## **Diagnosis & Management**

### Genetic Testing Information

- What is genetic testing?  
[/primer/testing/genetic-testing](#)
- Genetic Testing Registry: Gillespie syndrome  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C0431401/>

### Research Studies from ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22Gillespie+syndrome%22+OR+%22Aniridia%22>

### Other Diagnosis and Management Resources

- Eunice Kennedy Shriver National Institute of Child Health and Human Development: How Do Health Care Providers Diagnose Intellectual and Developmental Disabilities?  
<https://www.nichd.nih.gov/health/topics/idds/conditioninfo/diagnosed>
- Eunice Kennedy Shriver National Institute of Child Health and Human Development: What Are Treatments for Intellectual and Developmental Disabilities?  
<https://www.nichd.nih.gov/health/topics/idds/conditioninfo/cure>

### **Additional Information & Resources**

#### Health Information from MedlinePlus

- Encyclopedia: Intellectual Disability  
<https://medlineplus.gov/ency/article/001523.htm>
- Health Topic: Developmental Disabilities  
<https://medlineplus.gov/developmentaldisabilities.html>
- Health Topic: Eye Diseases  
<https://medlineplus.gov/eyediseases.html>

#### Genetic and Rare Diseases Information Center

- Gillespie syndrome  
<https://rarediseases.info.nih.gov/diseases/13/gillespie-syndrome>

#### Educational Resources

- American Association for Pediatric Ophthalmology and Strabismus  
<https://aapos.org/terms/conditions/26>
- Centers for Disease Control and Prevention: Developmental Disabilities  
<https://www.cdc.gov/ncbddd/developmentaldisabilities/>
- MalaCards: gillespie syndrome  
[https://www.malacards.org/card/gillespie\\_syndrome](https://www.malacards.org/card/gillespie_syndrome)
- Minnesota Department of Health  
<http://www.health.state.mn.us/divs/cfh/topic/diseasesconds/aniridia.cfm>
- Orphanet: Aniridia-cerebellar ataxia-intellectual disability syndrome  
[https://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=1065](https://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1065)
- Swedish Information Centre for Rare Diseases  
<http://www.socialstyrelsen.se/rarediseases/gillespiesyndrome>
- The University of Arizona Health Sciences  
<https://disorders.eyes.arizona.edu/disorders/gillespie-syndrome>

### Patient Support and Advocacy Resources

- Aniridia Europe  
<https://www.aniridia.eu/what-is-aniridia/>
- National Organization for Rare Disorders (NORD)  
<https://rarediseases.org/rare-diseases/aniridia-cerebellar-ataxia-mental-deficiency/>
- The Arc: For People with Intellectual and Developmental Disabilities  
<https://www.thearc.org/>

### Scientific Articles on PubMed

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

### Catalog of Genes and Diseases from OMIM

- GILLESPIE SYNDROME  
<http://omim.org/entry/206700>

### Medical Genetics Database from MedGen

- Gillespie syndrome  
<https://www.ncbi.nlm.nih.gov/medgen/96563>

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