

# CHARGE SYNDROME

## GENETIC TESTING



## What is CHARGE syndrome?

Each year, about 1 in 10,000 babies worldwide is born with a complex pattern of birth defects known as CHARGE syndrome.<sup>1</sup> The specific features of CHARGE syndrome include the following<sup>1,2</sup>:

- **C** = coloboma (defects) in parts of 1 or both eyes that may cause vision loss
- **H** = heart defects
- **A** = atresia of the choanae (narrowing or blockage of the breathing passages in the nose) that make breathing and swallowing difficult
- **R** = retardation of growth and development
- **G** = genital tract abnormalities
- **E** = ear abnormalities and hearing loss

Newborns with CHARGE syndrome often have many life-threatening health conditions.<sup>2</sup> Defects in the cranial nerve, which controls the muscles in the head and neck, are another common feature of CHARGE syndrome.<sup>1,2</sup> These defects can make swallowing difficult, and feeding disorders are a common cause of death in affected people of all ages.<sup>2</sup>

Management of CHARGE syndrome may include surgical insertion of a tube into the trachea to help with breathing, surgery to open the breathing passages in the nose and/or repair heart defects, feeding therapy, hearing aids, and psychological and school evaluations.<sup>2</sup>

## What causes CHARGE syndrome?

More than half of all cases of CHARGE syndrome are caused by an abnormal change in a gene called *CHD7*.<sup>3</sup> Genes are found in every cell in your body. They carry the instructions for making proteins that control how each of your cells work. Genes can undergo abnormal changes (called mutations) that may cause cells to stop working the way they should. Gene mutations may result in health conditions, and they may be passed from parent to child (inherited).

The *CHD7* gene contains the instructions for a protein that is believed to control gene expression in fetal tissues, including the eye, inner ear, and certain parts of the brain. Gene expression is the process by which genes become proteins that allow cells to perform their specific functions. When the *CHD7* gene is altered, the *CHD7* protein does not work the way it should, gene expression in fetal tissues is abnormal, and the pattern of defects seen in CHARGE syndrome may result.

## How is CHARGE syndrome inherited?

Normally, each of your cells carries 2 copies of all your genes. You inherit 1 copy of a gene from each of your parents. CHARGE syndrome is inherited in an autosomal dominant manner.<sup>2</sup> That means a child only needs to inherit 1 copy of gene mutation known to cause CHARGE syndrome in order to be affected with the disorder.

- Most cases of CHARGE syndrome arise from *de novo* mutations.<sup>2</sup> This means the gene mutation occurs for the first time in the affected child instead of being passed from parent to child.
- If 1 parent of an affected child has CHARGE syndrome or a *CHD7* mutation, then there is a 50% chance that the affected child's brothers and sisters (siblings) will inherit the mutation.<sup>2</sup>
- If neither parent of an affected child is affected, there is a 1% to 2% chance that the affected child's siblings will have CHARGE syndrome.<sup>2</sup>

## How is CHARGE syndrome diagnosed?

Your doctor will follow specific guidelines to diagnose CHARGE syndrome. Those guidelines are based on the identification of the presence of certain "major" and "minor" features of the disorder, which are shown in Table 1. Either all 4 of the major features **or** 3 major and 3 minor features must be present in order to confirm a diagnosis of CHARGE syndrome.<sup>1,2</sup>

Because the features of CHARGE syndrome overlap with some other genetic disorders<sup>1</sup>, your doctor may recommend a genetic test called gene sequencing to confirm the diagnosis of CHARGE syndrome.

**Table 1: Major and Minor CHARGE Syndrome Features**

Major Features	Minor Features
Ocular coloboma	Incomplete development of the genitals
Narrowing or blockage of the breathing passages in the nose	Delayed developmental milestones
Cranial nerve abnormalities or defects	Slow growth
Ear abnormalities	Cleft lip or palate
	Abnormal passageway between the trachea and the esophagus
	Facial deformities

### What is gene sequencing for CHARGE syndrome?

Gene sequencing for CHARGE syndrome is a procedure that reads the instructions (DNA) that makes up the *CHD7* gene. This test, which is performed on a sample of blood, is a way to identify the presence of mutations in the *CHD7* gene, which can help a doctor<sup>2</sup>:

- Confirm a diagnosis of CHARGE syndrome.
- Distinguish CHARGE syndrome from other genetic disorders that can cause similar birth defects.
- Determine close relatives of an affected child may be at risk for CHARGE syndrome.

### What possible results of gene sequencing can be reported, and what might they mean?

- **Negative:** After assessing the *CHD7* gene, no mutations were found. A negative result may reduce the chance that a child has CHARGE syndrome but cannot completely rule it out.

- **Positive:** After assessing the *CHD7* gene, a mutation was found, confirming the diagnosis of CHARGE syndrome.
- **Variant of unknown significance:** After assessing the *CHD7* gene, a mutation was found that either has not been reported before, or previous reports about the mutation have been conflicting. Therefore, it is unclear if the mutation is the cause of the child's signs and symptoms. Genetic testing of family members may provide more information. If all affected family members have the same mutation, then it is likely to be linked to the inherited disorder. If some affected family members do not have the mutation, it is less likely to be linked to the disorder.

Gene sequencing test results should be combined with clinical findings and reviewed by a health professional who specializes in medical genetics.

### Where can I find more information?

If you have questions or want more information about genetic testing for CHARGE syndrome, ask your doctor or genetic counselor. You may search for a genetic counselor in your area using an online address book provided by the National Society of Genetic Counselors at [www.nsgc.org](http://www.nsgc.org).

Other information resources include:

- The CHARGE Syndrome Foundation  
Telephone: 800 442-7604  
Home page: [www.chargesyndrome.org](http://www.chargesyndrome.org)
- Genetics Home Reference  
Home page: <http://ghr.nlm.nih.gov>

**Note:** This material is provided for general information purposes only. It is not intended as a substitute for medical advice and/or consultation with a physician or technical expert.

#### References

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