Leber Congenital Amaurosis

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Contributor: Camila Xu

Leber congenital amaurosis is an eye disorder that primarily affects the retina, which is the specialized tissue at the back of the eye that detects light and color. People with this disorder typically have severe visual impairment beginning in infancy. The visual impairment tends to be stable, although it may worsen very slowly over time.

genetic conditions

1. Introduction

Leber congenital amaurosis is also associated with other vision problems, including an increased sensitivity to light (photophobia), involuntary movements of the eyes (nystagmus), and extreme farsightedness (hyperopia). The pupils, which usually expand and contract in response to the amount of light entering the eye, do not react normally to light. Instead, they expand and contract more slowly than normal, or they may not respond to light at all. Additionally, the clear front covering of the eye (the cornea) may be cone-shaped and abnormally thin, a condition known as keratoconus.

A specific behavior called Franceschetti's oculo-digital sign is characteristic of Leber congenital amaurosis. This sign consists of poking, pressing, and rubbing the eyes with a knuckle or finger. Researchers suspect that this behavior may contribute to deep-set eyes and keratoconus in affected children.

In rare cases, delayed development and intellectual disability have been reported in people with the features of Leber congenital amaurosis. However, researchers are uncertain whether these individuals actually have Leber congenital amaurosis or another syndrome with similar signs and symptoms.

At least 13 types of Leber congenital amaurosis have been described. The types are distinguished by their genetic cause, patterns of vision loss, and related eye abnormalities.

2. Frequency

Leber congenital amaurosis occurs in 2 to 3 per 100,000 newborns. It is one of the most common causes of blindness in children.

3. Causes

Leber congenital amaurosis can result from mutations in at least 14 genes, all of which are necessary for normal vision. These genes play a variety of roles in the development and function of the retina. For example, some of the genes associated with this disorder are necessary for the normal development of light-detecting cells called photoreceptors. Other genes are involved in phototransduction, the process by which light entering the eye is converted into electrical signals that are transmitted to the brain. Still other genes play a role in the function of cilia, which are microscopic finger-like projections that stick out from the surface of many types of cells. Cilia are necessary for the perception of several types of sensory input, including vision.

Mutations in any of the genes associated with Leber congenital amaurosis disrupt the development and function of the retina, resulting in early vision loss. Mutations in the *CEP290*, *CRB1*, *GUCY2D*, and *RPE65* genes are the most common causes of the disorder, while mutations in the other genes generally account for a smaller percentage of cases. In about 30 percent of all people with Leber congenital amaurosis, the cause of the disorder is unknown.

3.1. The genes associated with Leber congenital amaurosis

- CEP290
- CRB1
- CRX
- GUCY2D
- RPE65

4. Inheritance

Leber congenital amaurosis usually has an autosomal recessive pattern of inheritance. Autosomal recessive inheritance 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.

When Leber congenital amaurosis is caused by mutations in the *CRX* or *IMPDH1* genes, the disorder has an autosomal dominant pattern of inheritance. Autosomal dominant inheritance means one copy of the altered gene in each cell is sufficient to cause the disorder. In most of these cases, an affected person inherits a gene mutation from one affected parent. Other cases result from new mutations and occur in people with no history of the disorder in their family.

5. Other Names for This Condition

- amaurosis, Leber congenital
- congenital amaurosis of retinal origin
- congenital retinal blindness
- CRB
- dysgenesis neuroepithelialis retinae
- hereditary epithelial dysplasia of retina
- hereditary retinal aplasia
- heredoretinopathia congenitalis
- LCA
- Leber abiotrophy
- Leber congenital tapetoretinal degeneration
- Leber's amaurosis

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