



Leber congenital amaurosis (LCA) is a genetic condition that causes severe loss of vision at birth or early childhood. LCA causes childhood blindness in 1:33,330 people. Recent scientific discoveries have helped us better understand LCA. Clinical trials testing therapies for some types of LCA have begun.

Early Symptoms

The symptoms of LCA are often noticed very early in a child's life – in the first weeks or months after birth. The parents may observe that the child does not focus on things in his/her environment. They may note that their child has “wobbly” back and forth eye movements called nystagmus. Some children may press or push on their eyes with their fingers or fist.

Medical Description

LCA is caused by a genetic mutation in one of several different genes. Each mutation has somewhat different characteristics. During an eye exam, the retina of a small child with LCA may not look different than a normal retina however further testing will reveal that the light-sensing photoreceptors in the retina are not sending electrical signals to the brain correctly.

Children with LCA usually have severe vision loss of 20/400 or worse. (A person with 20/400 vision can see at 20 feet what a person with normal vision can see at 400 feet). Some children may have only light/dark perception or rarely, no vision at all.

Children with some vision may have other symptoms such as night blindness or light sensitivity. They also may be far-sighted.

There are rare genetic syndromes that mimic LCA vision loss in young children. These include Alström syndrome, Batten disease, Joubert syndrome, and peroxisomal diseases (Zellweger

syndrome or Refsum disease). Children with these conditions have vision loss similar to LCA, along with other physical/ mental disabilities.

A child diagnosed with true LCA (not one of the syndromes above) may, in rare cases, be more vulnerable to kidney disease than other children. However, compared to the general population, they do not have a greater risk of either intellectual disabilities or autism.

Genetic Causes

Mutations in at least 15 different genes are known to cause LCA. Thirteen of these have been named LCA types 1-13:

Type	Gene	% of cases
LCA 1	GUCY2D	12
LCA 2	RPE65	6
LCA 3	SPATA7	Unknown
LCA 4	AIPL1	5
LCA 5	Lebercillin	2
LCA 6	RPGRIP1	4
LCA 7	CRX	1
LCA 8	CRB1	10
LCA 9	Unknown	Unknown
LCA 10	CEP290	15
LCA 11	IMPDH1	8
LCA 12	RD3	0.1
LCA 13	RDH12	3

Mutations in the LRAT, MERTK1 and TULP1 genes can also cause LCA.

Diagnosis

An ERG (electroretinography) is the most important test for diagnosing LCA. It rules out other cause of early vision loss. **OCT** (optical coherence tomography) which makes digital images of the retinal layers may also be suggested.

ERG testing may be done on one or both eyes. Drops are put in the eye and the child must stay in a dark room for at least 30 minutes. Large contact lenses are inserted into the eye and it is exposed to flashes of light. This can be done under anesthesia, if need-be. The eye's electrical response to light is measured. Children with LCA usually have no detectable electrical response from either the rod or cone photoreceptors. This is important for the diagnosis, but it does not mean that the photoreceptors are dead.

To rule out the syndromes mentioned earlier, other testing may also be recommended. Genetic testing gives a definitive diagnosis of LCA, if a mutation listed on page 1 is found. In 25-30% of cases the genetic cause cannot yet be determined. Ongoing research continues to identify new genetic mutation.

Treatment

No treatments are currently approved for LCA however research is very hopeful. Both gene and drug therapy are giving positive results in human trials of patients with specific mutations. Some types of LCA are associated with cataracts and changes to the cornea. It may be possible to treat these conditions and restore some vision, thus it is important for people with LCA to be monitored often.

What to Expect

LCA vision loss varies from child to child but remains stable over time in 75% of cases. About 15% will have progressive vision loss, while 10% may experience modest, often temporary, improvement.

Research

Some people with LCA are experiencing improved vision by using the Argus II retinal prosthesis. The Foundation is helping to support the Canadian trial of this device.

Gene Therapy for RPE65 mutations

In 2007, the first clinical trial of a gene therapy for defects in the RPE65 gene began. Since then about 30 people have been treated in clinical trials; all appear to have had at least some benefit with no serious side effects. Trials are ongoing. To learn more, see our gene therapy fact sheet.

Drug therapy for RPE65 and LRAT

These two genetic mutations impair the ability of the retina to convert vitamin A into a substance necessary for vision called 11-cis-retinal. In this clinical trial, sponsored by the Canadian company QLT Inc, participants take an oral retinoid called QLT091001. This trial began at the Montreal Children's Hospital of the McGill University Health Centre under the direction of Dr. Robert Koenekoop; recently several other trial sites have opened in the US and Europe. **In July, 2014, the trial published very encouraging results. 10 of the 14 people involved in the trial experienced visual improvements, including expanded visual fields and better visual acuity.**

Gene therapies for other genetic types of LCA (e.g., GUCY2D, AIPL1, and RPGRIP1) are also being developed. Additional research teams are targeting other genes and it is anticipated that more clinical trials will start in the next few years.

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