Leber congenital amaurosis

What is Leber congenital amaurosis?

Leber congenital amaurosis (LCA) is a form of inherited retinal disease (IRD) that appears at birth or within in the first few months of life. The extent of vision loss varies from person to person but can be quite severe (with little to no light perception).

LCA is an umbrella term given to a group of diseases that are caused by mutations in at least 18 known genes. The gene mutations lead to failure in the function of the photoreceptor cells (rod and cones cells that receive light), ultimately causing vision loss. Given the severity of the condition, it is one of the most extensively researched inherited retinal disorders.

LCA can be caused by several different genes, including *RPE65*, which can be treated using the approved gene therapy Luxturna® (voretigene neparvovec-rzyl). However, there are other genetic causes of LCA for which there are not currently any treatments.

How is Leber congenital amaurosis identified?

The retinal appearance of Leber congenital amaurosis (LCA) can be very similar to a generic retinitis pigmentosa appearance, and diagnosis can be tricky. One diagnostic clue is that in most cases of LCA, a particular form of imaging called fundus autofluorescence imaging (FAF) is darker than normal. In most cases, a definitive diagnosis of LCA will require genetic testing.

What are the symptoms of Leber congenital amaurosis?

There are many different types of Leber congenital amaurosis (LCA), and the disease can present differently in different children. However, there are some basic symptoms that are often associated with LCA.

These include:

- nystagmus (involuntary jerky rhythmic eye movements)
- poor vision or blindness
- strabismus (crossed eyes)
- photophobia (extreme sensitivity to light) and
- slow or no pupillary response to light.

Eye pressing and rubbing the eyes with a knuckle or finger can be common with babies and children who have very little vision. They do this as pressing on the eyeball causes them to perceive lights and colours, which is very appealing to small children. However, this can cause damage to the cornea (keratoconus) and lens and may result in a loss of fatty tissue around the eyes causing the eyes to look deep set.

The extent of degeneration depends on the type of LCA the child has, and for some types of LCA the vision remains stable.

What is the cause of Leber congenital amaurosis and how is it inherited?

- Leber congenital amaurosis (LCA) is a very rare condition which is estimated to affect around 1 in 80,000 people. [1]
- Forms of LCA are caused by a mutation in one of a number of genes that are important for the development and function of the retina, resulting in vision loss or blindness. [1]
- It is usually inherited in an autosomal recessive manner. However, there are rare incidences where the inheritance pattern may be autosomal dominant.

What treatments are available?

For Leber congenital amaurosis caused by mutations in the *RPE65* gene, there is now a gene therapy, Luxturna®, that has been approved for clinical use by the US Food and Drug Administration (FDA, USA), National Institute for Health Care and Excellence (NICE, UK) and the Therapeutic Goods Administration (TGA) in Australia.

The *RPE65* gene is involved in the production of a protein essential for the functioning of the retina. Luxturna® delivers a functional copy of the RPE65 gene to the retina, restoring the production of the protein and improving vision.[2] The treatment involves a one-time injection of the therapy into the affected eye, with the benefits expected to last for life.

It is important to note that Luxturna® is only effective for LCA caused by *RPE65* mutations and is not suitable for other genetic causes of LCA. Also, as with any medical treatment, there are potential risks and side effects associated with Luxturna®, and it should only be administered by qualified healthcare professionals. Currently, the two locations in Australia where Luxturna® treatment is available are the Sydney Eye Hospital (team led by Dr John Grigg) and the Royal Victorian Eye and Ear Hospital (team led by Dr Thomas Edwards).

To know if you are eligible for this treatment, an ophthalmologist will complete an eye examination and genetic testing to confirm.

A number of emerging treatments are being developed for LCA caused by other genes that may assist people in the future.

References
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(2)Russell S, Bennett J, Wellman JA, et al. Efficacy and safety of voretigene neparvovec (AAV2-hRPE65v2) in patients with RPE65 -mediated inherited retinal dystrophy: a randomised, controlled, open-label, phase 3 trial. The Lancet. 2017;390(10097):849-860. doi:10.1016/s0140-6736(17)31868-8

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