RETINA australia

Leber hereditary optic neuropathy (LHON)

Leber hereditary optic neuropathy (LHON) is a genetic disease that leads to sudden vision loss during young adult life. Men are more likely to be affected than women. LHON is a disorder caused by mutations in the genetic code of the mitochondria, which are small subunits that reside within the cell.

Mitochondria are also known as the “powerhouses of the cell” as they constantly convert energy locked in our food into energy that the cell can use. Our eyes are our most energy hungry organs and a lack of energy production can lead to degeneration and death of retinal ganglion cells (RGCs), which are the nerve cells that communicate visual information to the brain. Loss of these cells leads to subsequent degeneration of the optic nerve and visual loss.

However, it is worth noting that a significant percentage of people who possess a mutation that causes LHON do not develop any features of the disorder. Loss of vision due to LHON does not cause any eye pain, but it is quite an alarming experience as the loss of central vision presents suddenly and can progress quite quickly, leaving only peripheral vision. This means that the majority of people with LHON retain independent mobility but cannot focus on anything straight ahead or see fine detail.

What are the symptoms of LHON?

Affected individuals do not usually present any symptoms until they develop visual blurring affecting their central vision. These vision problems may begin in one eye or both simultaneously. If one eye is affected, then similar symptoms appear in the other eye on average eight weeks later. Over time, the vision in both eyes worsens with a severe loss of sharpness and a fading of colour vision.

The vision loss mainly affects central vision, which is needed for tasks such as reading, driving and recognising faces. In a small percentage of cases, the central vision loss can improve; but in most cases loss of vision is permanent. The severity of symptoms may vary from one affected individual to another, even within the same family, due to a 'dosage' effect. This is due to the fact that we have many mitochondria in each cell.

In one individual, if only a small proportion of mitochondria in each cell have the mutation, symptoms will be mild. In another individual, if a higher proportion of mitochondria in each cell carry the mutation, symptoms will be more severe.

What is the cause of LHON and how is it inherited?

LHON follows a mitochondrial pattern of inheritance, which is also known as maternal inheritance. Only egg cells and not sperm cells contribute mitochondria to a developing embryo, therefore only females can pass mitochondrial conditions to their children. Fathers affected by LHON, or carrying LHON, mutations do not pass the condition to their children. Often, people who develop LHON have no family history of the condition. However, it

is currently impossible to predict which members of a family who carry a mutation will eventually develop vision loss.

More than 50% of men and more than 85% of women with a mitochondrial mutation will never experience vision loss. LHON is a very rare condition. Exact prevalence is unknown in Australia, but it is thought to affect between one in 30,000 to one in 50,000 individuals worldwide. Research has revealed that three particular mutations in mitochondrial genes account for between 85% – 90% of cases of LHON.

What treatments are available?

Currently, there are no approved treatments or cures for LHON. There is strong evidence that environmental factors such as smoking and excessive alcohol consumption are linked to why some susceptible people develop the condition and others do not. Therefore, many actions that contribute to a healthy lifestyle should be adopted by those at risk. A number of new therapies are also in development for the treatment of LHON, including pharmaceutical compounds and gene therapies.

There is a growing body of evidence to suggest that idebenone, an antioxidant compound initially developed for the treatment of Alzheimer's disease, may be effective in the treatment of LHON. Studies have found that idebenone is effective during the earliest phase of symptoms and protects from further retinal ganglion cell loss. Other antioxidants are currently being examined for their protective effects on the retina.

A number of research teams are investigating gene-based therapies for the treatment of LHON. Gene therapies that target the cell nucleus have been successfully employed in other retinal conditions, however progress in LHON has been slower as there is a need to deliver such a therapy targeted to the mitochondria, of which there may be hundreds or thousands within a single cell. Many of these barriers have now been overcome however and progress in LHON gene therapy can be expected to progress over the coming years.