RETINA australia

Usher syndrome

Usher syndrome refers to a group of genetic conditions that have both hearing loss and progressive deterioration in vision due to retinitis pigmentosa (RP). While patients with retinitis pigmentosa do have a greater tendency to develop hearing difficulties as they age compared to the general population, the term Usher syndrome is reserved for patients where the hearing loss becomes obvious at a very early age.

The vision loss aspect of the syndrome is due to a form of retinitis pigmentosa which affects the photoreceptor cells, which are responsible for capturing images from the visual field. Usher syndrome causes a gradual decline in vision because two types of photoreceptor cells, known as the rod and cone cells, begin to degenerate and die.

Usher syndrome is responsible for the majority of cases of deaf-blindness, but the rate of progression of vision loss can vary widely from person to person and even within members of the same family. Some people with Usher syndrome may also have problems with their balance.

What are the symptoms of Usher syndrome?

The major symptoms of Usher syndrome are hearing loss and an eye disorder called retinitis pigmentosa, or RP. Deafness is the first symptom to become apparent, usually from birth.

There are broadly three different clinical types of Usher syndrome: type 1, type 2, and type 3. In Australia, types 1 and 2 are the most common types. People with Usher type 1 develop profound deafness from birth and early childhood symptoms of RP. The deafness is generally so early in onset and so severe that hearing aids may not be of value (although cochlear implants may be beneficial), and patients fail to develop intelligible speech.

Patients with Usher type 2 also have an early onset hearing loss but the deafness is less severe than in type 1 and thus the child will benefit from hearing aids and will develop intelligible speech. In type 2 Usher syndrome the features of RP usually become obvious during their teenage years.

Usher type 3 is a very rare form of Usher and is generally found in people with their family origins in Finland.

What is the cause of Usher syndrome and how is it inherited?

The prevalence of Usher syndrome varies from country to country, but it is a rare condition affecting approximately one in 10,000 people. Usher syndrome is a genetic disease that occurs when there are mutations (defects) in genes that are important for the function of both photoreceptors in the retina and hair cells in the cochlea, or inner ear.

So far, researchers have found 11 genes that are associated with the three main subtypes of the syndrome. Usher syndrome is always inherited in a recessive pattern. Patients with a combination of early-onset partial deafness and retinitis pigmentosa but due to alterations in the mitochondrial DNA do not fall into the category of Usher syndrome.

If a family member is diagnosed with Usher syndrome, it is strongly advised that other members of the family also have an eye exam by an eye doctor (ophthalmologist) who is specially trained to detect retinal diseases. As the deafness becomes obvious at a much earlier age than the RP in patients with Usher syndrome, it is particularly important that younger siblings with a hearing problem have a careful eye examination.

What treatments are available?

Current treatment focuses on helping an individual to adapt to hearing and vision loss and to maximising the vision and hearing that they do have. This includes the use of hearing aids, assistive listening devices, cochlear implants, mobility training, and low vision services. The wide range of assistive technologies available provides plenty of choice for users at all stages of sight and hearing loss and this technology has also removed many barriers to education and employment.

Prospects for the development of effective Usher syndrome treatments have never been brighter. The syndrome is passed down through a recessive pattern of inheritance with only one pair of genes affected and is therefore a prime candidate for gene therapy.

Gene therapy involves using harmless viruses to deliver and insert a healthy copy of the gene into the retina, thereby restoring function. This approach has led to exciting initial results in a number of other retinal diseases.

Usher syndrome gene therapy is quite challenging as the genes affected tend to be extremely large in size and difficult to deliver. However, scientists are exploring other harmless viruses that have the ability to safely deliver these large genes. One trial is currently in the early stages of recruitment in the USA and France, and more trials are planned in the future. Research into Usher syndrome is also being undertaken in Australia.

Retina Australia has awarded a 2019 grant to Dr Livia Carvalho from the Lions Eye Institute in Perth for a project called “Dual AAV retinal gene therapy approach for Usher 1F treatment”. Dr Carvalho was a guest speaker at our 2015 Retina Australia conference in Melbourne, and we look forward to hearing her speak about this work at a future national conference. Some forms of Usher syndrome are due to mutations known as “nonsense” mutations that lead to the incomplete and premature production of essential proteins.

There are now new drugs in the very early stages of testing for a number of other rare genetic conditions due to nonsense gene mutations that may have the potential to stop the defective protein synthesis and produce the correct form of the protein.

Neuroprotective agents that aim to preserve the function of the rod and cone photoreceptor cells for longer also hold huge potential for Usher syndrome, by maintaining a small, but significant amount of central vision.

Many of the therapies that are in development will not bring back the lost vision that occurs due to Usher syndrome, but they do have the potential to slow down or halt further degeneration, until other therapies, such as the exciting developments that have occurred in stem cell research, become available.

Efforts at transplanting stem cell derived photoreceptor cells are still at an early stage of research, however, a number of recent animal studies have shown the potential to restore function in the eye, which may pave the way for human studies in the future. Despite the lack of current treatments for Usher syndrome, general eye check-ups are important. This is because people with Usher syndrome are still at risk for other kinds of eye problems that can affect the general population, such as cataracts, and may be treatable.

Regular visits to your eye doctor can also make you aware of current advances as we learn more about these conditions.