



**RETINA**  
australia

### **Stargardt disease**

Stargardt disease is the most common form of inherited juvenile macular degeneration and it affects the portion of the retina known as the macula. The macula is the central portion of the retina. It contains photoreceptor cells known as cone cells, which are responsible for central (reading) vision and for colour vision.

Stargardt disease, also known as fundus flavimaculatus, is usually diagnosed in individuals under the age of 20 when decreased central vision is first noticed; for example a person may have difficulty seeing the board in class. The progression of visual loss varies hugely between individuals, but side or peripheral vision is usually preserved. This means that patients with Stargardt disease rarely have issues with independent mobility.

### **What are the symptoms of Stargardt disease?**

Central vision is usually the first affected, and the first symptom is often difficulty reading. Blind spots can occur, and these may increase in size over time. The condition can be slowly degenerative and progressive, but it is very uncommon for someone with Stargardt disease to become completely blind.

Both eyes are usually affected in a similar manner and colour vision may be affected in the later stages of disease. The rate of progression and degree of visual loss can vary from person to person and even among affected members of the same family. It is, therefore, very difficult to predict what an individual's vision will be like at a specific time in the future.

### **What is the cause of Stargardt disease and how is it inherited?**

The prevalence of Stargardt disease worldwide is estimated to be one in 8,000 to one in 10,000 and in Australia this equates to approximately 2500 – 3000 affected individuals. The majority of people with Stargardt disease have the recessive form of disease, involving mutations in the ABCA4 gene, which provides instructions to make the ABCA4 protein. If there is a faulty ABCA4 gene, it leads to the build-up of a toxic waste product known as A2E in the retinal pigment epithelium (RPE), and can lead to macular degeneration and progressive loss of vision.

A very rare form of Stargardt disease may be caused by mutations in the ELOVL4 gene, which follows an autosomal dominant form of inheritance. Mutations in the ELOVL4 gene can make dysfunctional ELOVL4 protein clumps that can interfere with photoreceptor cell functions leading to cell death. If a family member is diagnosed with Stargardt disease, 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.

## **What treatments are available?**

At present, there are no effective treatments for Stargardt disease. There is research to suggest that UV sunlight can increase the toxicity of the waste products accumulating in the retina, therefore, it is recommended that people with Stargardt disease wear UV screening sunglasses when out in direct sunlight. Recent evidence also suggests that taking extra vitamin A, such as in a vitamin supplement, may have a negative effect on the condition and should be avoided. Gene therapy is currently being explored for the recessive form of Stargardt disease caused by ABCA4 mutations.

The idea behind gene therapy is that a “normal” copy of the ABCA4 gene can be engineered in the laboratory. This can then be injected into the eye of an affected individual, delivering the correct copy of the gene and therefore stopping the degeneration of the sight of the individual. This approach is underway in a clinical trial in the USA and France, in order to find out if this is a safe approach.

There is also a follow-up study examining the condition of the retina in the years after treatment. Stem cells are amazing cells that are produced in the body and have the remarkable potential to develop into many different cell types in the body during early life and growth.

A number of groups worldwide are currently manipulating stem cells from various origins in order to produce retinal pigment epithelial (RPE) and these cells have been injected into a number of patients. To date, these cells have proven to be safe and well tolerated. The transplantation of these functional

cells into patients may prevent the death of the remaining photoreceptors and may, therefore, help Stargardt patients avoid further sight loss.

These early stage clinical trials are currently on-going. Efforts at transplanting stem cell-derived photoreceptor cells are at an even earlier stage of research, but 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. Another interesting approach that is currently being studied as a therapy involves research into a modified form of vitamin A, called deuterated vitamin A. The researchers hope that this may help slow the accumulation of A2E by blocking its formation downstream in the visual cycle.

They are currently testing the safety of this approach. Please note however that recent evidence suggests that taking extra “normal” vitamin A, such as in a vitamin supplement from a health shop, may have a negative effect on the condition and should be avoided as this can increase toxic levels of A2E.

Despite the lack of current treatments for Stargardt disease, general eye check-ups are important. This is because people with Stargardt disease are still at risk for other kinds of eye problems that can affect the general population and may be treatable. Regular visits to your eye doctor can also make you aware of current advances and new treatments as we learn more about the condition. How to live with Stargardt Disease. It may be very hard to deal with a diagnosis of Stargardt disease.

Many people have never heard of the disease and are unsure how Stargardt disease will affect them. It is important to realize that most of the time the disease progresses slowly. For the most part, you will not have to learn new skills overnight. People who have Stargardt disease lead successful and full lives. There are people to help you along the way. Many kinds of services are available if and when they are needed.

It is perfectly natural for someone with vision loss to feel anxious, fearful, angry, or unhappy. If your child has Stargardt disease, it is also natural to have feelings of uncertainty, anxiety, and fear over what the future may hold for him or her. It is critical that you discuss these feelings with your medical team. Support groups can also be very helpful.