

**What is X-Linked Retinoschisis?**

X-linked retinoschisis (XLRS) is an inherited disease diagnosed in childhood that causes progressive loss of central and peripheral (side) vision due to degeneration of the retina. XLRS affects tens of thousands of people all over the world. Approximately 35,000 people in the United States and Europe have the condition.

**What are the symptoms?**

XLRS occurs most frequently in males. Although the condition begins at birth, symptoms do not typically become apparent until after the age of 10. About half of all patients diagnosed with retinoschisis first notice a decline in vision. Other early symptoms of the disease include an inability of both eyes to focus on an object (strabismus) and roving, involuntary eye movements (nystagmus).

Vision loss associated with

juvenile retinoschisis is caused by the splitting of the retina into two layers. This retinal splitting most notably affects the macula, the central portion of the retina responsible for perceiving detail and colors. On examination, the fovea (the center of the macula) has spoke-like streaks. The spaces created by the separated layers are often filled with blisters and ruptured blood vessels that can leak blood into the vitreous body (the transparent, colorless mass of jelly-like material filling the center of the eye). The presence of blood in the vitreous body causes further visual impairment. The

**The Foundation publishes updates on the latest advancements in research for retinoschisis and similar diseases.**

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vitreous body degenerates and may eventually separate from the retina. The entire retina may also separate from underlying tissue layers causing retinal detachments.

The extent and rate of vision loss vary greatly among patients with XLRS. Central vision is almost always affected. Peripheral (side) vision loss occurs in about half of all cases. Some patients retain useful vision well into adulthood, while others experience a rapid decline during childhood.

### **Is it an inherited disease?**

XLRS is genetically passed through families by the X-linked pattern of inheritance. In this type of inheritance, the gene for the disease is located on the X chromosome. Females have two X chromosomes and can carry the disease gene on one of their X chromosomes. Because they have a healthy copy of the gene on their other X chromosome, carrier females are often not affected by X-linked diseases such as XLRS. However, in recent years, more females have been identified with

having vision loss from X-linked conditions.

Males have only one X chromosome (paired with one Y chromosome) and are therefore genetically susceptible to X-linked diseases. Males affected with an X-linked disease always pass the gene on the X chromosome to their daughters, who then become carriers. Affected males never pass an X-linked disease gene to their sons, because fathers pass the Y chromosome to their sons.

Female carriers have a 50 percent chance (or 1 chance in 2) of passing the X-linked disease gene to their daughters, who become carriers, and a 50 percent chance of passing the gene to their sons, who are then affected by the disease.

### **What treatment is available?**

Researchers are currently working toward launching a clinical trial of gene therapy for XLRS. Gene therapies work by delivering copies of healthy genes to the retina to replace the defective

copies that are causing vision loss. In collaboration with a Foundation-funded research team at Oregon Health & Science University, Applied Genetic Technologies Corporation (AGTC) is developing a gene therapy based on an adeno-associated virus (AAV) for XLRS. The company's goal is to submit an Investigational New Drug (IND) application to the U.S. Food and Drug Administration to begin a clinical trial in 2015. Formal safety studies in small and large animal models required for IND submission are planned. A natural-history study of people with XLRS has also been initiated to identify the best measures for evaluating treatment efficacy.

The Foundation is funding other research projects to identify compounds that can preserve vision. Future stem cell treatments might also benefit people with retinoschisis.

A recent study showed that a drug called dorzolamide may improve retinal health and restore some vision in people with retinoschisis.

Individuals with XLRS may also benefit from the use of low-vision aids, including electronic, computer-based and optical aids. Orientation and mobility training, adaptive training skills, job placement and income assistance are available through community resources.

### **Are there any other related diseases?**

XLRS can resemble other retinal degenerative diseases such as retinitis pigmentosa (RP), Goldman-Favre vitreoretinal dystrophy, Wagner's vitreoretinal dystrophy, and Sticklers syndrome. A thorough ophthalmologic examination, including diagnostic tests measuring retinal function and visual field, combined with an accurate documentation of family history, can distinguish between these diseases. Genetic testing can also provide a definitive diagnosis.