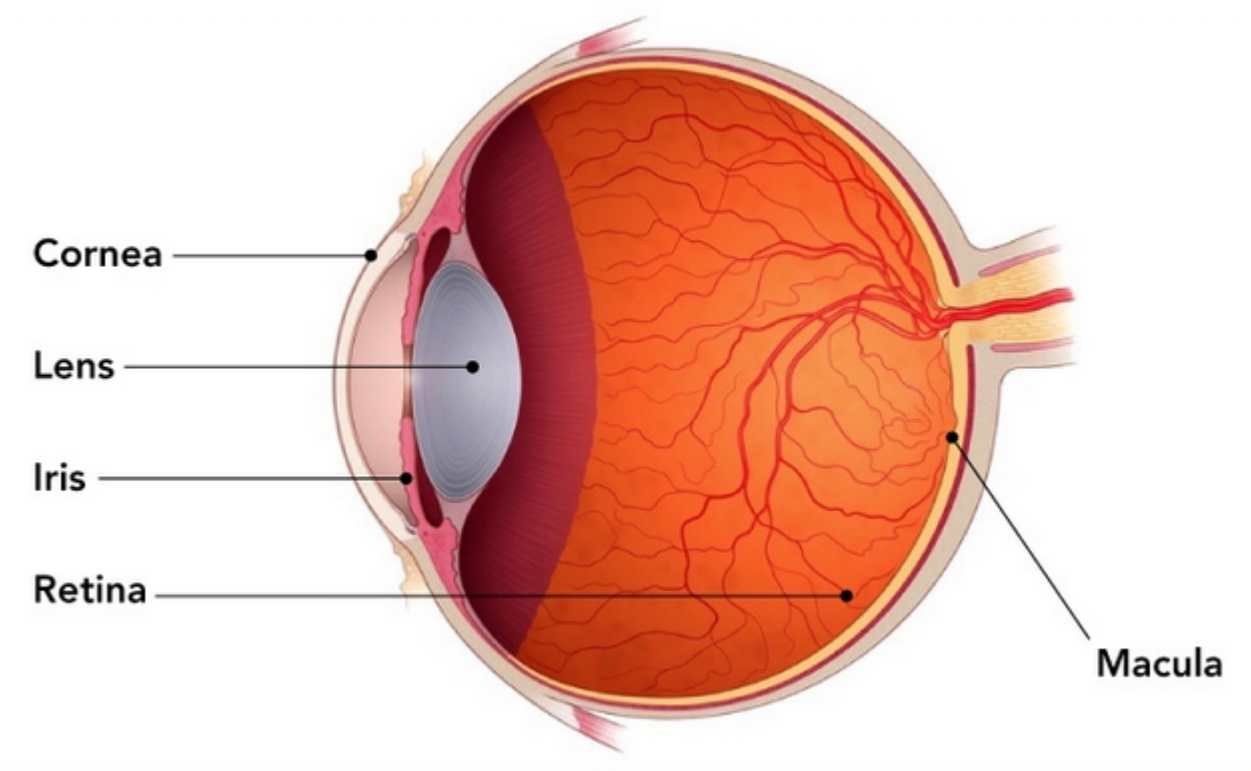

Source: https://clinicaoftalmologicacimo.es/

Retinoblastoma is rare cancer that starts in the retina. The retina is the region on the back of the eye which senses light and sends messages to the brain. Retinoblastoma most commonly occurs in early childhood. It may occur in one eye (unilateral) or in both eyes (bilateral). The first sign of this cancer is often leukocoria (the white reflection of light when looking at the pupil of the eye) or strabismus (one “crossed” or outwardly gazing eye).

Ninety percent of children diagnosed with retinoblastoma in one eye have no family history of this type of cancer. While for many of these children their cancer developed sporadically by chance, there is a possibility for each child diagnosed with retinoblastoma to have a genetic predisposition as the cause for their cancer. Because of this possibility, all children diagnosed with retinoblastoma should be offered genetic counseling to discuss the option of genetic testing. The likelihood of a genetic explanation increases if the cancer occurs in multiple spots within the same eye (multifocal), if the cancer occurs in both eyes, or there is a family history of retinoblastoma.

There are no external risk factors (such as cigarette smoking or alcohol exposure) that are

confirmed to cause retinoblastoma.

Genetics and Inheritance

We have over 20,000 different genes in the body. These genes are like instruction manuals for how to build a protein, and each protein has an important function that helps to keep our body working how it should. Pathogenic (or harmful) variants in the *RB1* gene cause hereditary retinoblastoma. The *RB1* gene makes a protein called pRB. The pRB protein is a tumor suppressor, which means that it works in the body to make sure that cells do not grow out of control. When someone does not have enough of this pRB protein in their body, cells can grow out of control, which is what can lead to cancers like retinoblastoma.

Pathogenic variants in the *RB1* gene are inherited in an autosomal dominant pattern, meaning that children of someone who carries a pathogenic variant each have a 50% chance to inherit the variant and associated cancer risks. Women and men both have the *RB1* gene and have the same chances to inherit and pass down variants in these genes.

Genetic Testing for RB1

Genetic testing for pathogenic variants in the *RB1* gene is currently available, but there are a few different ways to approach testing:

- *Single site analysis*: Testing specific to a known pathogenic variant in the family
- Full gene sequencing and rearrangement analysis: Comprehensive testing to search for all currently detectable variants in the gene
- Chromosome microarray: Testing that looks for missing pieces of chromosome 13 (which is where the *RB1* gene is)

Risk of Cancer with RB1 gene mutations

Retinoblastoma

The majority of individuals who inherit a pathogenic variant in the *RB1* gene will develop cancer in both of their eyes. Fortunately, retinoblastoma is usually curable when detected early. Retinoblastoma is most likely to occur within the first few years of life. Children who have a pathogenic variant in the *RB1* gene should have surveillance under anesthesia every 3 – 4 weeks within the first 6 months of life. Children should then have an eye exam every 3-6 months until age 7. After age 7, these exams can be spaced out to every 1-2 years.

Pinealblastoma

Five and a half percent of people with pathogenic variants in the *RB1* gene will develop a tumor in the “retina like” pineal gland of the brain (referred to a *trilateral* retinoblastoma). A regular MRI of the brain can be done for young children to screen for this.

Other cancers

There is an elevated risk of some cancers outside of the eye, including tumors of the bone (osteosarcoma) and the soft tissue of organs. The onset of these other cancers may be in childhood or adulthood. Because of this, regular total body MRI screening might be recommended for people with pathogenic variants in the *RB1* gene.

Melanoma skin cancer also occurs more frequently in individuals with *RB1* pathogenic variants, and a regular skin check is recommended.

People with a *RB1* pathogenic variant have a sensitivity to radiation, so avoiding radiation therapy (CT scans and x-rays) unless absolutely necessary can be helpful to reduce the chance for a second cancer.

Click here to learn more about scheduling a genetic counseling appointment for questions about hereditary cancer predisposition.

Additional Resources

*Positive Results Facebook Group
Genetic Support Foundation hosts a Facebook group for Hereditary Cancer Support and Resources. Get trusted information and join a community of support.
*Cascade Screening Connector
Genetic Support Foundation has partnered with the Washington State Department of Health to provide cascade screening to help people identify and contact family members who may have an increased chance of developing cancer.
*FORCE (Facing Our Risk of Cancer Empowered)
The FORCE mission is to improve the lives of individuals and families facing hereditary cancer. Resources include peer navigation and expert-reviewed information.
*AliveAndKicknAliveAndKickn is a nonprofit working to improve the lives of individuals and families affected by Lynch Syndrome and associated cancers through research, education, and screening.
*Health Experiences USAThis national research project brings patient voices into the healthcare experience and features video clips of people facing hereditary cancer.

Individuals from a variety of backgrounds share both positive and negative experiences about living with hereditary cancer.
Children's Oncology Group
Children's Cancer Web
National Cancer Institute
Cancer.net