Retinoblastoma

The earlier the childhood eye cancer is detected, the greater the chances of cure.

Learn how to recognize the signs and symptoms of this disease, which affects young children and may occur in one or both eyes.

Retinoblastoma is a cancer that affects young children. It is most common in infants, and approximately 90% of cases are diagnosed before 5 years of age.

It is a tumor that develops in the retina, the inner layer of the eye responsible for vision. When diagnosed early and treated at specialized centers, cure rates can exceed 90%. However, prognosis becomes significantly worse when the disease spreads beyond the eye.

Early diagnosis of retinoblastoma not only increases the chances of survival, but may also preserve the child's vision and the eye itself.

This booklet was developed to help parents, healthcare professionals, grandparents, caregivers, teachers, and everyone who has direct contact with children recognize the warning signs of this disease.

We hope this information will be helpful.

What is Retinoblastoma?

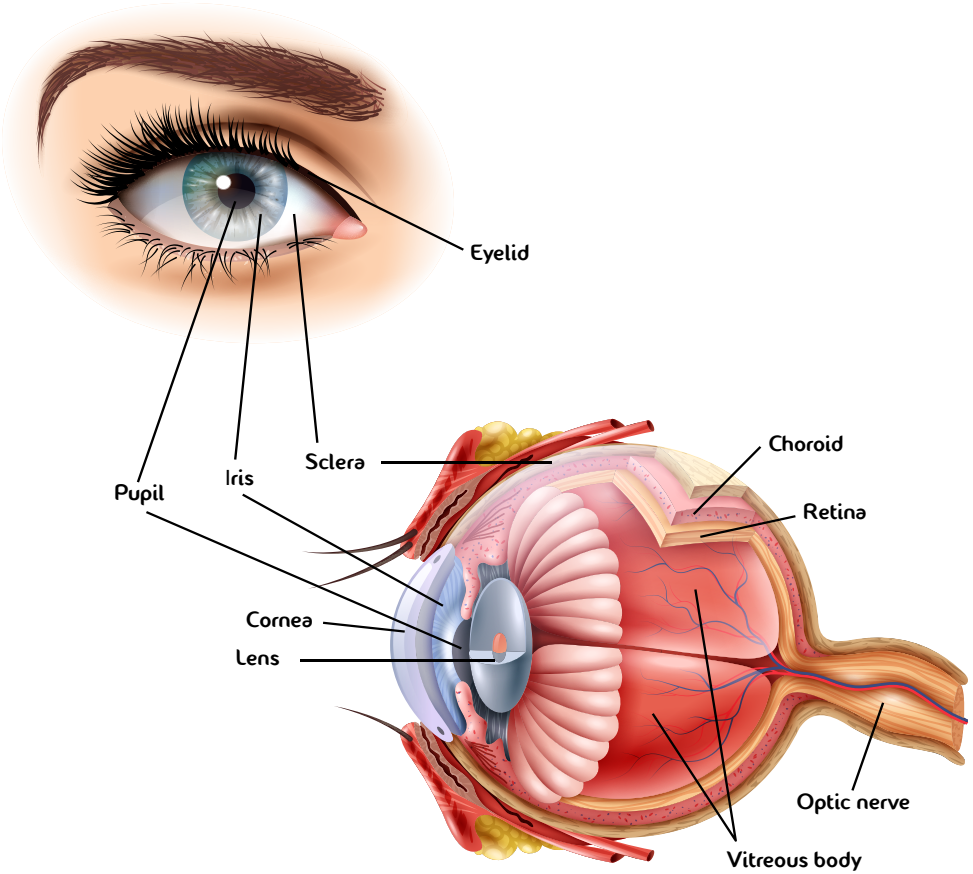
Retinoblastoma is the most common primary intraocular malignant tumor in childhood. It accounts for approximately 14% of all cancers diagnosed in children under 2 years of age. It is a rare disease, with approximately 7000 to 8000 new cases diagnosed annually in the world. More than 90% of cases occur in children between 0 and 5 years of age, with most diagnoses made around 2 years old. There is no difference in incidence between boys and girls, among ethnic groups, or between the right and left eye. The disease may affect one eye (unilateral retinoblastoma – approximately 60% of cases) or both eyes (bilateral retinoblastoma – approximately 40% of cases). When diagnosed early, retinoblastoma is highly curable and vision may often be preserved. However, delayed diagnosis can result in blindness, spread of the disease beyond the eye, and even death.

Understanding the Eye

Sclera – the white outer layer that protects the eye

Choroid – the vascular middle layer that nourishes the eye

Retina – the inner layer containing photoreceptor cells responsible for vision; this is where retinoblastoma develops



Red Reflex and Leukocoria

The red reflex is seen when light passes through the pupil and reflects from the retina and choroid, producing a normal reddish-orange glow. When this reflex appears white instead of red, it is called leukocoria (from the Greek leukos = white, kore = pupil), commonly known as the "cat's eye reflex." Leukocoria may affect one or both eyes and can be associated with several pediatric eye diseases, including:

- Cataract
- Uveitis
- Persistent fetal vasculature
- Retinopathy of prematurity
- Coats disease
- Retinoblastoma

↳ **1.**Leukocoria is present in approximately 60–80% of retinoblastoma cases.

↳ **2.** Retinoblastoma is the most serious disease among the causes of leukocoria.

Any abnormality in the red reflex should be considered a warning sign and prompt immediate medical evaluation. Changes may include absence of the reflex or an abnormal white or orange reflex. The red reflex test performed at the maternity ward, together with regular ophthalmologic examinations during early childhood, allows early diagnosis of several eye diseases and helps reduce childhood blindness and visual impairment.

Clinical Forms of Retinoblastoma

Unilateral Retinoblastoma

Approximately 60% of children with retinoblastoma have disease affecting only one eye, usually with a single tumor focus. This form is commonly diagnosed around 2 years of age and is generally non-hereditary.

Bilateral or Multifocal Retinoblastoma

This presentation is usually associated with the hereditary form of retinoblastoma and accounts for approximately 40% of cases. In hereditary retinoblastoma, one copy of the RB1 gene is altered during fetal development and is therefore present in all cells of the body. This is known as a germline mutation. As a result, these children tend to develop tumors at an earlier age, often in both eyes and in multiple locations within the retina. Because all body cells carry the altered RB1 gene, these patients also have a higher risk of developing secondary cancers later in life. A small number of children may also develop a tumor in the brain, most commonly in the pineal gland (pineoblastoma), a condition known as trilateral retinoblastoma.

Genetics

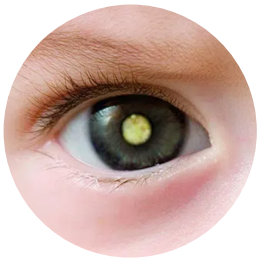
The development of retinoblastoma is a complex process that begins with alterations in the RB1 gene. The normal RB1 gene produces a protein that functions as a tumor suppressor, helping regulate cell growth and programmed cell death. When both copies of the RB1 gene become altered or inactivated, retinal cells can grow uncontrollably, leading to the development of retinoblastoma.

How to Recognize the Signs and Symptoms

Retinoblastoma is often first suspected when parents or physicians notice an abnormal appearance in the child's eye.

The main signs and symptoms include:

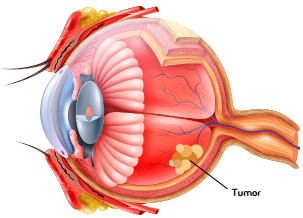
White pupillary reflex (Leukocoria)



Also known as the "cat's eye reflex," leukocoria is the most common sign of retinoblastoma. Normally, when light shines into the eye, the pupil appears red because of the reflection from the choroid. In eyes affected by retinoblastoma, a white reflection may be seen instead. This white reflex is often noticed in photographs taken with flash and may also be identified during routine eye examinations.

Strabismus ("crossed eyes")

Strabismus occurs when the eyes are not properly aligned and do not look in the same direction. Although many conditions may cause strabismus, retinoblastoma is one of the possible causes and should always be considered.



Other less common signs and symptoms

- Decreased vision
- Abnormal eye movements
- Eye pain
- Redness of the eye
- Bulging of the eye
- Difference in iris color between the eyes

How is Retinoblastoma Suspected?

Fundus examination is the recommended screening test for detecting retinoblastoma in asymptomatic children. However, the disease is frequently first noticed by parents or identified during pediatric examinations. During routine evaluations, pediatricians observe the appearance of the eyes, eye movements, and visual behavior. Any abnormal finding may suggest retinoblastoma or another ocular condition. Parents or caregivers may notice that the child's eye does not appear normal, especially after seeing a white reflex in photographs. Awareness of the warning signs and symptoms is essential so that medical evaluation can be obtained as early as possible.

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1. A detailed fundus examination under anesthesia is performed to carefully evaluate both eyes.
2. Magnetic resonance imaging (MRI) of the brain and orbits is important to assess possible extraocular extension and optic nerve involvement, as well as to help differentiate retinoblastoma from other ocular diseases.

Treatment

Treatment of retinoblastoma is complex and requires a specialized multidisciplinary team. Treatment planning is individualized and depends on:

- the child's age,
- whether the disease affects one or both eyes,
- tumor size and location,
- and the extent of the disease.

In most cases, multiple treatment modalities are combined for the same patient.

Current Treatment Modalities

Laser Therapy

Laser therapy uses highly focused light beams to heat and destroy retinoblastoma tumors.

Brachytherapy

Brachytherapy uses localized internal radiation delivered through a radioactive plaque surgically attached to the eye wall. Iodine-125 and Ruthenium-106 are among the most commonly used radioisotopes in ocular brachytherapy.

Cryotherapy

Cryotherapy destroys tumor cells by freezing them with an extremely cold probe.

Enucleation

Enucleation is the surgical removal of the eye and may be necessary in advanced cases.

Chemotherapy

Chemotherapy reduces tumor volume and allows consolidation with focal therapies such as laser therapy, cryotherapy, and brachytherapy. Treatment modalities include:

1. Systemic chemotherapy
    - ↳ Carboplatin + Etoposide (Vepesid) + Vincristine (VEC)
2. Intravitreal chemotherapy
3. Intra-arterial chemotherapy

Newer treatment techniques, such as intravitreal chemotherapy and selective ophthalmic artery chemotherapy, aim to increase drug concentration within the eye while reducing systemic side effects.

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Technical Data

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This booklet is supportive material and does not replace a specialized medical consultation.

Medical-scientific support

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