About Retinoblastoma

Overview

If your child has been diagnosed with retinoblastoma or you are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- What Is Retinoblastoma?

Research and Statistics

See the latest estimates for new cases of retinoblastoma in the US and what research is currently being done.

- Key Statistics for Retinoblastoma
- What's New in Retinoblastoma Research?

What Is Retinoblastoma?

Cancer starts when cells begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas. To learn more about how cancers start and spread, see What Is Cancer?[1] For information about the differences between childhood cancers and adult cancers, see Cancer in Children[2].

Retinoblastoma is a cancer that starts in the retina, the very back part of the eye. It is the most common type of eye cancer in children. Rarely, children can have other kinds

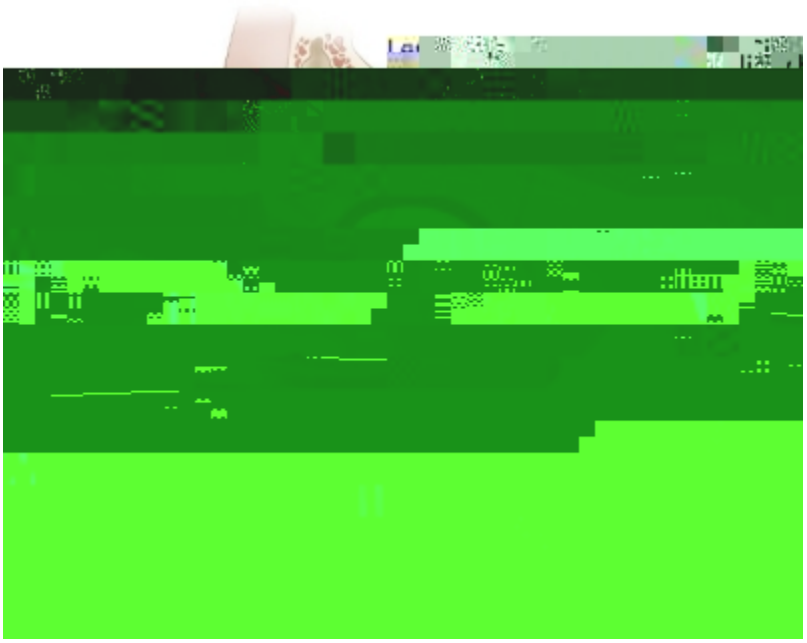
of eye cancer, such as medulloepithelioma, which is described briefly below, or ocular (eye) melanoma[3].

To understand retinoblastoma, it helps to know how the parts of the eye work.

The eye

The main part of the eye is the eyeball (also known as the **globe**), which is filled with a jelly-like material called **vitreous humor**. The front of the eyeball has a clear lens with an iris (the colored part of the eye that acts like a camera shutter), which allows light to enter the eye and focuses it on the retina.

The retina is the inner layer of cells in the back of the eye. It is made up of special nerve cells that are sensitive to light. These light-sensing cells are connected to the brain by the optic nerve, which runs out the back of the eyeball. The pattern of light (image) that reaches the retina is sent through the optic nerve to an area of the brain called the visual cortex, allowing us to see.



How does retinoblastoma develop?

The eyes start to develop well before birth. During the early stages of development, the eyes have cells called **retinoblasts**, which multiply to make new cells that fill the retina. At a certain point, these cells stop multiplying and become mature retinal cells.

Rarely, something goes wrong with this process. Instead of maturing, some retinoblasts continue to grow out of control, forming a cancer known as retinoblastoma.

The chain of events inside cells that leads to retinoblastoma is complex, but it almost always starts with a change (mutation) in the *RB1* gene. The normal *RB1* gene helps keep cells from growing out of control, but a change in the gene stops it from working like it should. Depending on when and where the change in the *RB1* gene occurs, it can result in 2 different types of retinoblastoma.

Congenital (heritable) retinoblastoma

In about 1 out of 3 children with retinoblastoma, the abnormality in the *RB1* gene is congenital (present at birth) and is in all the cells of the body, including all of the cells of both retinas. This is known as a **germline mutation**.

Despite this sometimes being called 'heritable' (or 'hereditary'), in most of these children, there is no family history of this cancer, and the *RB1* gene change is not inherited from a parent. In these children, the gene change first occurs during early development in the womb. Only a small portion of the children born with this gene change inherit it from a parent.

Children born with a mutation in the *RB1* gene usually develop retinoblastoma in both eyes (known as **bilateral retinoblastoma**), and there are often several tumors within the eye (known as **multifocal retinoblastoma**).

Because all of the cells in the body have the changed *RB1* gene, these children also have a higher risk of developing cancers in other parts of the body.

- A small number of children with this form of retinoblastoma will develop another tumor in the brain, usually in the pineal gland at the base of the brain (a pineoblastoma). This is also known as **trilateral retinoblastoma**.
- For survivors of hereditary retinoblastoma, the risk of developing other cancers later in life is also higher than average (to learn more, see After Treatment for Retinoblastoma[4]).

Sporadic (non-heritable) retinoblastoma

In about 2 out of 3 children with retinoblastoma, the abnormality in the *RB1* gene develops in only one cell in one eye. It is not known what causes this change. A child who has sporadic (non-heritable) retinoblastoma develops only one tumor in one eye.

This type of retinoblastoma is often found when the child is slightly older compared with those who have the heritable form.

Children with this type of retinoblastoma do not have the same increased risk of other cancers as children with congenital retinoblastoma.

For more on the heritable and non-heritable forms of retinoblastoma, see What Causes Retinoblastoma?[5]

How does retinoblastoma grow and spread?

If retinoblastoma tumors are not treated, they can grow and fill much of the eyeball. Cells might break away from the main tumor on the retina and reach other parts of the eye, where they can form more tumors. These tumors might block the channels that let fluid circulate within the eye, raising the pressure inside the eye. This can cause glaucoma, which can lead to pain and loss of vision in the affected eye.

Most retinoblastomas are found and treated before they have spread outside the eyeball. But if they are not, retinoblastoma cells can spread to other parts of the body. The cells sometimes grow along the optic nerve and reach the brain. Retinoblastoma cells can also grow through the covering layers of the eyeball and into the eye socket, eyelids, and nearby tissues. Once the cancer is outside the eyeball, it can then spread to lymph nodes[6] (small bean-sized collections of immune system cells) and to other organs such as the liver, bones, and bone marrow (the soft, inner part of many bones).

Intraocular medulloepithelioma

Medulloepithelioma is a very rare type of tumor that can start in the eye. It is not a type of retinoblastoma, but it's mentioned here because it also usually occurs in young children.

Medulloepitheliomas start in the ciliary body, which is near the front of the eye (see image above). Most of these tumors are malignant (cancerous), but they rarely spread outside the eye. They usually cause eye pain and loss of vision.

The **diagnosis** is made when a doctor finds a tumor in the eye by using an ophthalmoscope (an instrument that helps doctors to look inside the eye). As with retinoblastoma, the diagnosis is usually made based on where the tumor is inside the eye and how it looks. A biopsy (removing cells from the tumor to be looked at under a microscope) to confirm the diagnosis is almost never done because it might harm the eye or risk spreading the cancer outside of the eye.

are diagnosed with retinoblastoma each year in the United States.

Retinoblastoma is most common in infants and very young children. The average age of children is 2 when it is diagnosed. It rarely occurs in children older than 6.

About 3 out of 4 children with retinoblastoma have a tumor in only one eye (known as **unilateral retinoblastoma**). In about 1 case in 4, both eyes are affected (known as **bilateral retinoblastoma**).

Retinoblastoma occurs about equally in boys and girls and in different races and ethnicities. It also occurs equally in the right or left eye.

Overall, more than 9 out of 10 children in the United States with retinoblastoma are cured, but the outlook is not as good if the cancer has spread outside of the eye.

References

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What's New in Retinoblastoma Research?

Over the past few decades, research into retinoblastoma has led to many advances in treatment, which in turn has led to much higher cure rates and fewer side effects. Still, not all children are cured, and even those who are cured might still have long-term side effects from treatment, so more research is needed.

Research on retinoblastoma is being done at many medical centers, university hospitals, and other institutions around the world.

Genetics, genetic testing, and gene therapy

The defective gene responsible for nearly all retinoblastomas (the *RB1* gene[1]) was identified in 1986. This discovery, along with technical advances in finding DNA changes, has made genetic testing for heritable (hereditary) retinoblastoma possible.

A great deal of research has gone into figuring out how certain DNA changes in retinal cells cause them to become cancerous. Scientists understand these changes better for retinoblastoma than for most other cancer types. Although probably still years away, researchers hope that this understanding will one day lead to gene therapies, very specific treatments that can repair or counteract these DNA changes.

For example, researchers have found that an oncogene known as *SYK*

Radiation therapy

External radiation therapy can be used to treat retinoblastoma, but it can cause side effects because the radiation often reaches nearby tissues as well. This is especially important in children with hereditary retinoblastoma, whose cells are more likely to be damaged by radiation.

Newer forms of radiation therapy such as **intensity modulated radiation therapy (IMRT)** and **proton beam therapy** can better target the tumor and spare nearby normal tissues. These techniques, which are described in Radiation Therapy for Retinoblastoma[2], may help doctors limit the side effects from radiation therapy.

Focal treatments

Doctors continue to improve the techniques used for cryotherapy[3], laser therapy[4] (photocoagulation and thermotherapy), and other focal treatments. The goal is to kill tumor cells more precisely while sparing other parts of the eye.

Chemotherapy

Chemotherapy (chemo) has played a larger role in treating many retinoblastomas in recent years.

Systemic chemo: Chemo given into a vein (IV) is now commonly used to shrink tumors before local treatments such as cryotherapy or laser therapy. Chemo is also given to some children **after** the removal of the eye (known as adjuvant chemotherapy) to help prevent the recurrence of retinoblastoma outside the eye. Doctors are also studying the use of different chemo drugs, as well as new ways of combining currently used drugs, to try to improve how well chemo works.

Localized chemo: Doctors continue to improve upon newer ways of getting chemo into the eye, such as **intra-arterial chemo** and **intravitreal chemo**. These approaches let doctors get higher doses of chemo to the tumors while reducing many of the typical chemo side effects, and are quickly becoming part of the standard treatment for many retinoblastomas. These techniques are described in Chemotherapy for Retinoblastoma[5].

High-dose chemotherapy and stem cell transplant: A stem cell transplant (SCT) lets doctors give higher doses of chemo than could safely be given otherwise. (In the past, this type of treatment was commonly referred to as a bone marrow transplant.) Doctors are studying the use of this type of treatment in children with retinoblastoma that hasoblastomsThare c

spread outside the eye and who are unlikely to be cured with other treatments.

Chemo drugs can affect quickly dividing cells like those in the bone marrow, which is where new blood cells are made. Even though higher doses of these drugs might be more effective in treating tumors, they can't be given because they would cause severe damage to bone marrow cells, leading to life-threatening shortages of blood cells.

To try to get around this problem, the doctor may treat the child with high-dose chemo (sometimes along with radiation therapy) and then use a stem cell transplant to "rescue" the bone marrow.

To learn more about stem cell transplants, including how they are done, see Stem Cell Transplant for Cancer[6].

Oncolytic virus therapy

Researchers are also trying to find ways to take advantage of the gene changes in retinoblastoma cells to treat these tumors. One example is VCN-01, a virus that's been modified in the lab to infect and destroy cells that don't have working copies of the *RB1* gene (which includes the vast majority of retinoblastomas). This treatment is now being studied in the earliest phases of clinical trials.

Hyperlinks

1. www.cancer.org/cancer/retinoblastoma/causes-risks-prevention/what-causes.html
2. www.cancer.org/cancer/retinoblastoma/treating/radiation-therapy.html
3. www.cancer.org/cancer/retinoblastoma/treating/cryotherapy.html
4. www.cancer.org/cancer/retinoblastoma/treating/laser-therapy.html
5. www.cancer.org/cancer/retinoblastoma/treating/chemotherapy.html
6. www.cancer.org/treatment/treatments-and-side-effects/treatment-types/stem-cell-transplant.html

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