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.

- What Are the Key Statistics About Retinoblastoma?
- What’s New in Retinoblastoma Research and Treatment?

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 of the body. To learn more about how cancers start and spread, see What Is Cancer? For information about the differences between childhood cancers and adult cancers, see Cancer in Children.

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 melanoma.

To understand retinoblastoma, it helps to know about the parts of the eye and how they work.
About 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 develop very early as babies grow in the womb. During the early stages of development, the eyes have cells called retinoblasts that divide into new cells and fill the retina. At a certain point, these cells stop dividing and develop into mature retinal cells.

Rarely, something goes wrong with this process. Instead of maturing into special cells that detect light, some retinoblasts continue to divide and 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 a gene called the *retinoblastoma (RB1) gene*. The normal *RB1* gene helps keep cells from growing out of control, but the change in the gene stops it from working like it should. Depending on when and where the change in the *RB1* gene occurs, 2 different types of retinoblastoma can result.

**Congenital (hereditary) 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*.

In most of these children, there is no family history of this cancer. Only about 25% of the children born with this gene change inherit it from a parent. In about 75% of children the gene change first occurs during early development in the womb. The reasons for this are not clear.

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 areas as well.

- 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. (For more information, see the section What Happens After Treatment for Retinoblastoma?)

**Sporadic (non-hereditary) retinoblastoma**

In about 2 out of 3 children with retinoblastoma, the abnormality in the *RB1* gene develops on its own in only one cell in one eye. It is not known what causes this change. A child who has sporadic (non-hereditary) retinoblastoma develops only one tumor in one eye. This type of retinoblastoma is often found at a later age than the hereditary form.
Children with this type of retinoblastoma do not have the same increased risk of other cancers as children with congenital retinoblastoma.

**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 float through the vitreous to reach other parts of the eye, where they can form more tumors. If these tumors block the channels that let fluid circulate within the eye, the pressure inside the eye can rise. 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 retinoblastoma cells can occasionally 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 reaches tissues outside the eyeball, it can then spread to lymph nodes (small bean-shaped 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 another type of tumor that can start in the eye. It is not a type of retinoblastoma, but it is mentioned here because it also usually occurs in young children. These tumors are very rare.

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 mass in the eye by using an ophthalmoscope (an instrument that helps doctors to look inside the eye). Like 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.

Treatment for medulloepithelioma is almost always surgery to remove the eye. This usually gets rid of all of the cancer, as long as it was still only in the eye.
The rest of this document refers only to retinoblastoma.

- References
  See all references for Retinoblastoma

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What Are the Key Statistics About Retinoblastoma?

Retinoblastoma is a rare disease. Only about 200 to 300 children are diagnosed with retinoblastoma each year in the United States. It is more common in infants and very young children than in older children. The average age of children when they are diagnosed is 2. It rarely occurs in children older than 6.

About 3 out of 4 children with retinoblastoma have a tumor in only one eye. In about 1 case in 4, both eyes are affected.

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 with retinoblastoma are cured, but the outlook is not nearly as good if the cancer has spread outside of the eye.

- References
  See all references for Retinoblastoma

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What’s New in Retinoblastoma Research and Treatment?

Over the past few decades, research into retinoblastoma has led to great advances and much higher cure rates for this type of cancer. 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 counseling, and gene therapy

The defective gene responsible for nearly all retinoblastomas (the RB1 gene) was identified in 1986. This discovery, along with technical advances in finding DNA changes, has made genetic testing for 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 is overactive in retinoblastoma cells. Drugs that target the protein this gene makes are now being developed. Another gene called MDM4 also seems to be involved in the development of retinoblastoma, and drugs aimed at blocking its effects are being studied.

Recently, researchers have found that a very small portion of retinoblastomas don’t seem to have changes in the RB1 gene, but instead have too many copies of another gene called MYCN. It is not yet clear if these cancers are different in any important ways from those with RB1 gene changes.

Treatment

Research is building on the progress made in treating retinoblastoma over the past few decades.
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. 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 the section Radiation Therapy for Retinoblastoma, may help doctors limit the side effects from radiation therapy.

Other local treatments

Doctors continue to improve the instruments used for cryotherapy, laser therapy (photocoagulation), thermotherapy, and other local 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 chemotherapy

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

Localized chemotherapy

Chemo can help shrink most retinoblastomas, but when it’s given into the bloodstream it can cause side effects in different parts of the body. This limits the doses that can be given. Newer techniques help keep the chemo concentrated in the areas around the tumors. This can help doctors get higher doses of chemo to the tumors while reducing some of these side effects. Some of these techniques are described in the section Chemotherapy for Retinoblastoma.

Intra-arterial chemotherapy: In this approach, chemo is injected directly into the ophthalmic artery, the main artery feeding the eye, using a long, thin catheter. When intra-arterial chemotherapy is used, the dose of the chemo drug is much lower than
when it is given by vein, and the side effects related to the chemo are minimal.

**Intravitreal chemotherapy:** Some doctors are studying injecting chemotherapy directly into the jelly-like fluid inside the eyeball (the vitreous humor) to treat tumors that are widespread within the eye and not helped by other treatments. The main concern with this technique is that placing the needle into the eye to give the chemo might open a small hole that could allow tumor cells to spread outside of the eye, so doctors are being very cautious with this approach. Some doctors are studying the use of cryotherapy (using very cold temperatures) at the site of injection to limit this risk. Intravitreal chemotherapy is still in the early stages of testing.

- References
  See all references for Retinoblastoma

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