Retinoblastoma Early Detection, Diagnosis, and Staging

Detection and Diagnosis

Catching cancer early often allows for more treatment options. Some early cancers may have signs and symptoms that can be noticed, but that is not always the case.

- Can Retinoblastoma Be Found Early?
- Signs and Symptoms of Retinoblastoma
- How Is Retinoblastoma Diagnosed?

Stages of Retinoblastoma

After a cancer diagnosis, staging provides important information about the extent of cancer in the body and anticipated response to treatment.

- How Is Retinoblastoma Staged?

Questions to Ask About Retinoblastoma

Here are some questions you can ask the cancer care team to help you better understand your child's diagnosis and treatment options.

- What Should You Ask Your Child's Doctor About Retinoblastoma?

Can Retinoblastoma Be Found Early?

Retinoblastoma is a rare cancer, and there are no widely recommended screening tests to look for retinoblastoma in children without symptoms. Still, many retinoblastomas are found early by parents, relatives, or a child's doctor.
During children’s regular physical exams, doctors routinely check their eyes. Some of the things doctors look for include changes in how the eyes look (inside or outside), changes in how the eyes move, and changes in the child’s vision. Any of these might be a sign of retinoblastoma, although they are more often caused by something else.

Sometimes, a parent or relative may notice that a young child’s eye doesn’t look normal, prompting a visit to the doctor. It’s important for parents to be aware of the possible signs and symptoms of retinoblastoma, and to report anything unusual to the doctor as soon as possible. Most often the cause is something other than retinoblastoma, but it’s important to have it checked so that the cause can be found and treated right away, if needed.

For children in families known to carry an abnormal RB1 gene, or in families with a history of retinoblastoma who have not had genetic testing for the RB1 gene, doctors recommend regular eye exams during the first years of life to detect any tumors at an early stage. These children often have an eye exam a few days after birth, again at about 6 weeks of age, then every few months until at least age 5. The RB1 gene defect can be found by a special blood test, so most doctors now advise that children with parents or siblings with a history of retinoblastoma have this genetic test done during the first few weeks after birth. The results of the test then help define how often eye exams should be done.

Most hereditary retinoblastomas develop and are diagnosed in infants only a few months old. Usually, if tumors develop in both eyes, it happens at the same time. But in some children, tumors develop in one eye first, then a few months (or even years) later in the other eye. So even if retinoblastoma is diagnosed in only one eye, these children will still need regular exams of the other eye for several years after treatment.

If a child has retinoblastoma that is thought to be hereditary, many doctors also recommend magnetic resonance imaging (MRI) scans of the brain at regular intervals for up to 5 years to check for a trilateral retinoblastoma (a brain tumor such as a pineoblastoma). For more information, see the section How Is Retinoblastoma Diagnosed?

- References
  See all references for Retinoblastoma

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Signs and Symptoms of Retinoblastoma

Retinoblastomas nearly always occur in young children. They are often found when a parent or doctor notices a child's eye looks unusual.

**White pupillary reflex**

This is the most common early sign of retinoblastoma. Normally when you shine a light in the eye, the pupil (the dark spot in the center of the eye) looks red because of the blood vessels in the back of the eye. In an eye with retinoblastoma, the pupil often appears white or pink instead, which is known as a white pupillary reflex (or leukocoria).

This white glare of the eye may be noticed by a parent after a flash photograph is taken, especially if the pupils are different colors. It also might be noted by the child's doctor during a routine eye exam.

**Lazy eye**

Sometimes the eyes don't appear to look in the same direction, a condition often called lazy eye. (Doctros call this strabismus.) There are many possible causes of this in children. Most of the time lazy eye is caused by a mild weakness of the muscles that control the eyes, but it can also be caused by retinoblastoma.

**Other possible signs and symptoms**

Less common signs and symptoms of retinoblastoma include:

- Vision problems
- Eye pain
- Redness of the white part of the eye
- Bleeding in the front part of the eye
- Bulging of the eye
- A pupil that doesn’t get smaller when exposed to bright light
- A different color in each iris (the colored part of the eye)

Many of these signs and symptoms are more likely to be caused by something other than retinoblastoma. Still, if your child has any of these, check with your child's doctor.
so the cause can be found and treated, if needed.

- References
  See all references for Retinoblastoma

How Is Retinoblastoma Diagnosed?

Retinoblastomas are usually found when a child is brought to a doctor because he or she has certain signs or symptoms.

For most types of cancer, the diagnosis is made with a biopsy. During a biopsy, the doctor removes a sample from the tumor and sends it to a lab to be looked at under a microscope.

But biopsies are not usually done to diagnose retinoblastoma for 2 reasons. First, taking a biopsy specimen from a tumor in the eye can’t be done easily without harming the eye and risking spreading cancer cells outside the eye. Second, retinoblastoma can usually be diagnosed accurately without a biopsy by doctors who have experience with this disease, and it’s unlikely to be confused with other eye problems in children.

Medical history and physical exam

If your child has signs or symptoms of retinoblastoma, the doctor will examine your child’s eyes and get a complete medical history. The doctor will ask about the child’s symptoms and may ask about any family history of retinoblastoma or other cancers. This information is important when deciding if more tests and exams are needed. Your family history is also useful for determining whether other relatives could possibly pass the retinoblastoma (RB1) gene change on to their children or develop this cancer themselves (if they are young children) and might benefit from genetic counseling.

If a retinoblastoma is suspected, the doctor will refer you to an ophthalmologist (a doctor who specializes in eye diseases), who will examine the eye closely to be more certain
about the diagnosis. The ophthalmologist will use special lights and magnifying lenses to look inside the eye. Usually, the child needs to be under general anesthesia (asleep) during the exam so that the doctor can take a careful and detailed look.

If a diagnosis of retinoblastoma seems likely based on the eye exam, imaging tests will be done to help confirm it and to find out how far it may have spread within the eye and possibly to other parts of the body. Usually an ophthalmologist who specializes in treating cancers of the eye (called an ocular oncologist) will make the final determination. This doctor should also be part of the team of doctors treating the cancer.

**Imaging tests**

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive substances to create pictures of the inside of the body. Imaging tests may be done for a number of reasons, including:

- To help tell if a tumor in the eye is likely to be a retinoblastoma
- To determine how large the tumor is and how far it has spread
- To help determine if treatment is working

Children thought to have retinoblastoma may have one or more of these tests.

**Ultrasound**

Ultrasound uses sound waves to create images of tissues inside the body, such as the inner parts of the eye. For this test, a small ultrasound probe is placed up against the eyelid or eyeball. The probe gives off sound waves and detects the echoes that bounce off the tissues inside and around the eye. The echoes are converted by a computer into an image on a computer screen.

Ultrasound is one of the most common imaging tests for confirming the diagnosis of retinoblastoma. It is painless and does not expose the child to radiation, but the child may need to be given medicine to help keep them calm or even asleep so the doctor can get a good look at the eye. This test can be very useful when tumors in the eye are so large they prevent doctors from seeing inside the whole eye.

Optical coherence tomography (OCT) is a similar type of test that uses light waves instead of sound waves to create very detailed images of the back of the eye.

**Magnetic resonance imaging (MRI) scan**
MRI scans are often used for retinoblastomas because they provide very detailed images of the eye and surrounding structures without using radiation. This test is especially good at looking at the brain and spinal cord. Most children with retinoblastoma will have at least one MRI scan. For children with bilateral retinoblastomas (tumors in both eyes), many doctors continue to do MRI scans of the brain for several years after treatment to look for tumors of the pineal gland (sometimes called *trilateral retinoblastoma*).

Unlike CT scans (described next), MRI scans use radio waves and strong magnets to create images instead of x-rays. A contrast material called *gadolinium* may be injected into a vein before the scan to show details better.

MRI scans can take up to an hour. Your child may have to lie inside a narrow tube, which is confining and can be upsetting. Newer, more open MRI machines can help with this, but the test still requires staying still for long periods of time. The machines also make buzzing and clicking noises that may be disturbing. Young children may be given medicine to help keep them calm or even asleep during the test.

**Computed tomography (CT) scan**

CT scans use x-rays to make detailed images of parts of the body. CT scans can help determine the size of a retinoblastoma tumor and how much it has spread within the eye and to nearby areas.

Normally, either a CT or an MRI scan is needed, but usually not both. Because CT scans give off radiation, which might raise a child’s risk for other cancers in the future, most doctors prefer to use MRI. However, a CT scan can show deposits of calcium in the tumor much better than an MRI, which can be very helpful when the diagnosis of retinoblastoma is not clear.

Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around your child while he or she lies on a table. A computer then combines these pictures into images of slices of the part of the body being studied.

Before the scan, your child may get an IV (intravenous) injection of a contrast dye that helps better outline structures in the body. The dye can cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives. Rarely, more serious reactions like trouble breathing or low blood pressure can occur. Be sure to tell the doctor if your child has any allergies (especially to iodine or shellfish) or has ever had a reaction to any contrast material used for x-rays.
CT scans take longer than regular x-rays, but not as long as MRI scans. A CT scanner has been described as a large donut, with a narrow table that slides in and out of the middle opening. Your child will need to lie still on the table while the scan is being done. Your child may be given medicine to help them stay calm or even go to sleep during the test to help make sure the pictures come out well.

**Bone scan**

A bone scan can help show if the retinoblastoma has spread to the skull or other bones. Most children with retinoblastoma don’t need to have a bone scan. It is normally used only when there is a strong reason to think retinoblastoma might have spread beyond the eye.

For this test, a small amount of low-level radioactive material is injected into a vein (intravenously, or IV). (The amount of radioactivity used is very low and will pass out of the body within a day or so.) The material settles in abnormal areas of bone throughout the body over the course of a couple of hours. Your child then lies on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of the skeleton. Younger children may be given medicine to help them stay calm or even go to sleep during the test.

Areas of active bone changes appear as “hot spots” on the scan. These areas may suggest cancer is in an area, but other bone diseases can also cause the same pattern. To help tell these apart, other tests such as plain x-rays or MRI scans of the bone might be needed.

For more details on imaging tests, see [Imaging (Radiology) Tests](#).

**Other tests**

Other tests are not often needed for retinoblastomas, but they may be helpful in some situations.

**Biopsy**

For most cancers, a biopsy (removing a tissue sample from the tumor and looking at it under a microscope) is needed to make a diagnosis. Trying to biopsy a tumor at the back of the eye can often damage the eye and may spread tumor cells, so this is almost never done to diagnose retinoblastoma. Instead, doctors make the diagnosis based on eye exams and on imaging tests such as those listed above. This is why it is very
important that the diagnosis of retinoblastoma is made by experts.

**Lumbar puncture (spinal tap)**

Retinoblastomas can sometimes grow along the optic nerve, which connects the eye to the brain. If the cancer has spread to the surface of the brain, this test can often find cancer cells in samples of cerebrospinal fluid (the fluid that surrounds the brain and spinal cord). Most children with retinoblastoma don’t need to have a lumbar puncture. It is used mainly when there is a reason to think retinoblastoma might have spread into the brain.

For this test, the child is typically given anesthesia so they will be asleep and not move during the procedure. This can help ensure the spinal tap is done cleanly. The doctor first numbs an area in the lower part of the back over the spine. A small, hollow needle is then placed between the bones of the spine to withdraw a small amount of the fluid. The fluid is then looked at under a microscope to check for cancer cells.

**Bone marrow aspiration and biopsy**

These 2 tests may be done to see if the cancer has spread to the bone marrow, the soft, inner part of certain bones. These tests are usually not needed unless the retinoblastoma has grown outside the eye and doctors suspect that the cancer may have also spread through the bloodstream to the bone marrow.

The tests are typically done at the same time. The samples are usually taken from the back of the pelvic (hip) bone, but in some cases they may be taken from other bones.

In *bone marrow aspiration*, the skin over the hip and the surface of the bone may be numbed with a local anesthetic. This test can be painful, so the child will probably be given other medicines to reduce pain or even be asleep during the procedure. A thin, hollow needle is then inserted into the bone, and a syringe is used to suck out (aspirate) a small amount of liquid bone marrow.

*A bone marrow biopsy* is usually done just after the aspiration. A small piece of bone and marrow is removed with a slightly larger needle that is pushed down into the bone. Once the biopsy is done, pressure is applied to the site to help stop any bleeding.

The samples are then looked at under a microscope to see if they contain cancer cells.

- References
  See all references for Retinoblastoma
How Is Retinoblastoma Staged?

The stage of cancer describes how far it has spread. The outlook (prognosis) for children with retinoblastoma depends, to some extent, on the cancer’s stage. The stage is also an important factor in choosing treatment.

Retinoblastoma is staged based on the results of eye exams, imaging tests, and any biopsies that were done. These tests are described in How Is Retinoblastoma Diagnosed?

A staging system is a standard way for your child’s cancer care team to sum up how far a cancer has spread. Doctors use staging systems to predict the outlook for saving the child’s vision, as well as for survival and the likelihood that certain treatments will be effective.

Several detailed systems can be used to stage retinoblastoma (see below). But for practical purposes, when determining the best treatment options, doctors often divide retinoblastomas into 2 main groups:

- **Intraocular retinoblastoma**: The cancer is still within the eye.
- **Extraocular retinoblastoma**: The cancer has spread beyond the eye. Extraocular cancers can be divided further into *orbital retinoblastomas*, which have spread only to the eye socket, and *metastatic retinoblastomas*, which have spread to distant parts of the body, such as the brain or bone marrow.

In the United States, most retinoblastomas are diagnosed before they have spread outside the eye, so staging systems that apply only to intraocular retinoblastoma are used most often in this country. There are 2 staging systems for intraocular retinoblastomas.

It’s important to know that regardless of the stage, almost all children with intraocular retinoblastoma can be cured if they are properly treated. But the stage has a bigger impact on whether the affected eye (or the vision in the eye) can be saved.
The International Classification for Intraocular Retinoblastoma is the newer staging system, which takes into account what has been learned about the disease in recent decades. Most doctors now use this system. It divides intraocular retinoblastomas into 5 groups, labeled A through E, based on the chances that the eye can be saved using current treatment options.

**Group A**

Small tumors (3 millimeters [mm] across or less) that are only in the retina and are not near important structures such as the optic disc (where the optic nerve enters the retina) or the foveola (the center of vision).

**Group B**

All other tumors (either larger than 3 mm or small but close to the optic disc or foveola) that are still only in the retina.

**Group C**

Well-defined tumors with small amounts of spread under the retina (subretinal seeding) or into the jelly-like material that fills the eye (vitreous seeding).

**Group D**

Large or poorly defined tumors with widespread vitreous or subretinal seeding. The retina may have become detached from the back of the eye.

**Group E**

The tumor is very large, extends near the front of the eye, is bleeding or causing glaucoma (high pressure inside the eye), or has other features that mean there is almost no chance the eye can be saved.

**The Reese-Ellsworth staging system**
The Reese-Ellsworth system was developed in the 1960s, when most children were being treated with external beam radiation therapy (EBRT). While this is no longer a common treatment, some doctors may still use this system to classify retinoblastomas that have not spread beyond the eye. This system can help determine the likelihood of preserving vision while still treating the tumor.

Terms such as favorable, doubtful, and unfavorable used in this staging system refer to the likelihood that the cancer can be treated while preserving the affected eye. These terms do not refer to the likelihood of the child’s survival. Indeed, more than 9 in 10 children with intraocular retinoblastomas are cured. The major challenge is saving the vision in the affected eye.

To explain the groupings below, it helps to define a few terms. The optic disc is the end of the optic nerve where it is attached to the retina. Retinoblastomas are diagnosed by looking at the retina through an ophthalmoscope, so doctors can’t measure their size directly using a ruler. Instead they compare the size of the tumor with the size of the optic disc, which is usually about 1.5 millimeters (1/16 inch) across. For example, a tumor estimated to be 3 times the size of the disc (3 disc diameters or 3 DD) would be about 4.5 millimeters (3/16 inch) across.

The equator is an imaginary line that divides the front and back halves of the eyeball.

The Reese-Ellsworth staging system divides intraocular retinoblastoma into 5 groups. The higher the group number, from 1 to 5, the lower the chance of controlling the retinoblastoma or of saving the eye or any useful vision.

**Group 1 (very favorable for saving [or preserving] the eye)**

- 1A: one tumor, smaller than 4 disc diameters (DD), at or behind the equator
- 1B: multiple tumors smaller than 4 DD, all at or behind the equator

**Group 2 (favorable for saving [or preserving] the eye)**

- 2A: one tumor, 4 to 10 DD, at or behind the equator
- 2B: multiple tumors, with at least one 4 to 10 DD, and all at or behind the equator

**Group 3 (doubtful for saving [or preserving] the eye)**

- 3A: any tumor in front of the equator
- 3B: one tumor, larger than 10 DD, behind the equator
Group 4 (unfavorable for saving [or preserving] the eye)

- 4A: multiple tumors, some larger than 10 DD
- 4B: any tumor extending toward the front of the eye to the ora serrata (front edge of the retina)

Group 5 (very unfavorable for saving [or preserving] the eye)

- 5A: tumors involving more than half of the retina
- 5B: vitreous seeding (spread of tumors into the jelly-like material that fills the eye)

Other staging systems

Other staging systems that include both intraocular retinoblastomas and those that have spread beyond the eye (extraocular retinoblastomas) may be used by some doctors. These can be especially useful in countries where these cancers are more likely to have spread by the time they are found. For example, the American Joint Commission on Cancer (AJCC) staging system takes into account 3 key pieces of information:

- T: The size of the main (primary) tumor and how far it has grown within and outside of the eye
- N: Whether or not the cancer has reached the lymph nodes (small, bean shaped collections of immune cells, to which cancers sometimes spread)
- M: Whether or not the cancer has spread (metastasized) to distant parts of the body, such as the bone marrow, brain, skull, or long bones

This system can be used to describe the extent of retinoblastomas in detail, particularly for those that have spread outside the eye, which rarely happens in the United States.

Be sure to ask your child's doctor if you have any questions about the stage of your child's cancer.

- References
  See all references for Retinoblastoma

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What Should You Ask Your Child’s Doctor About Retinoblastoma?

It’s important to have honest, open discussions with your child’s doctors. You should ask any question on your mind, no matter how small it might seem. Here are some questions you might want to ask.

- What kind of eye cancer does my child have? Is it retinoblastoma?
- Is only one eye affected or are there tumors in both eyes?
- Has the tumor spread beyond the eye?
- What is the stage of the cancer, and what does that mean?
- Has my child’s vision been affected?
- Do we need other tests before we can decide on treatment?
- How much experience do you have treating this type of cancer?
- Do we need to see any other types of doctors?
- What are our treatment options?
- Can my child’s sight be saved? If so, how much?
- What do you advise and why?
- Are there any clinical trials we should consider?
- How long will treatment last? What will it be like? Where will it be done?
- What should we do to be ready for treatment?
- What are the risks and side effects of the suggested treatments?
- Which side effects start shortly after treatment and which ones might develop later on?
- Will treatment affect the growth of the area around my child’s eye?
- Will treatment affect my child’s ability to grow and develop?
- Could treatment affect my child’s ability to have children later on?
- What is the chance of curing the cancer?
- What would we do if the treatment doesn’t work or if the cancer comes back?
- Is there any risk of this type of tumor occurring in our other children or relatives?
- Should we consider genetic counseling and testing?
- What type of follow-up will my child need after treatment?
- Does my child have a higher long-term risk of other cancers?
Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so you can plan your schedules. You may also want to ask about getting a second opinion or if you can be put in touch with other families who have been through similar situations.

Also keep in mind that doctors are not the only ones who can give you information. Other health care professionals, such as nurses and social workers, may be able to answer some of your questions. You can find out more about speaking with your health care team in The Doctor-Patient Relationship.

- References

See all references for Retinoblastoma

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