Retinoblastoma

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*.

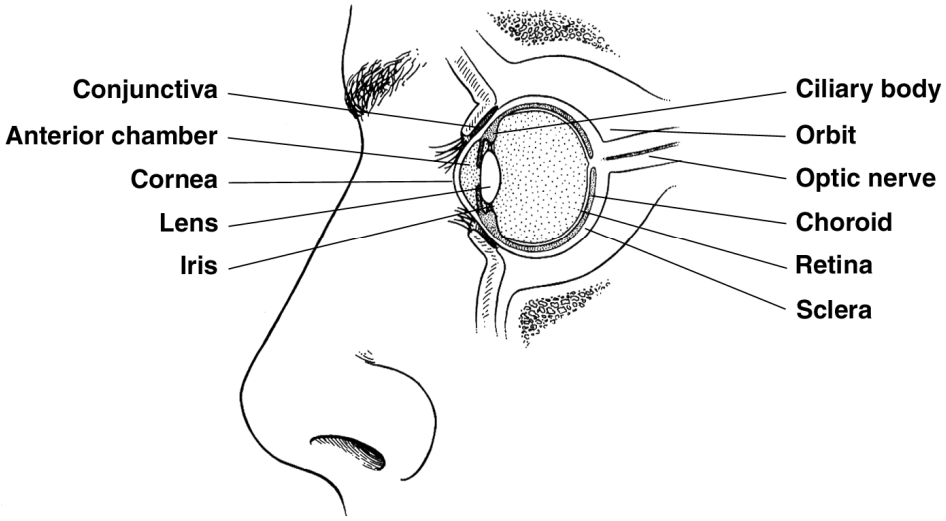
Retinoblastoma is a cancer that starts in the retina, the very back part of the eye. It is the most common type of eye cancer in children. Rarely, children can have other kinds of eye cancer, such as medulloepithelioma, which is described briefly below, or melanoma.

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.

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.

What are the risk factors for retinoblastoma?

A risk factor is anything that affects a person’s chance of getting a disease such as cancer. Different cancers have different risk factors.

Lifestyle-related risk factors such as body weight, physical activity, diet, and tobacco use play a major role in many adult cancers. But these factors usually take many years to influence cancer risk, and they are not thought to play much of a role in childhood cancers, including retinoblastomas.

There are very few known risk factors for retinoblastoma.

Age

Most children diagnosed with retinoblastoma are younger than 3 years old. Most congenital or hereditary retinoblastomas are found during the first year of life, while non-inherited retinoblastomas tend to be diagnosed in 1- and 2-year-olds. Retinoblastomas are rare in older children and in adults.

Heredity

About 1 out of 3 retinoblastomas is caused by a mutation (change) in the *RB1* gene that is present in all the cells of the child's body. But of these cases, only about 1 in 4 is inherited from one of the child's parents. In the rest, the gene mutation is not inherited, but occurs during early development in the womb. Children born with a mutation in the *RB1* gene usually develop retinoblastoma in both eyes. Regardless of whether the mutated *RB1* gene was inherited from a parent or not, because these children have the mutated gene in all of their cells, they have a 1 in 2 chance of eventually passing it on to their children.

Most of the remaining 2 out of 3 retinoblastomas occur as a result of a random *RB1* gene mutation that occurs only in one cell of one eye. These mutations are not inherited from a parent, and children who have them do not pass on a greatly increased risk of retinoblastoma to their children. Non-hereditary retinoblastomas always affect one eye only.

The way in which inherited gene changes make certain children likely to develop retinoblastoma is explained in the section "Do we know what causes retinoblastoma?"

Do we know what causes retinoblastoma?

Retinoblastoma is caused by mutations (changes) in certain genes. Over the past few decades, scientists have learned how certain changes in a person's DNA can cause cells of the retina to become cancerous. The DNA in each of our cells makes up our genes, which are the instructions for how our cells function. We usually look like our parents because they are the source of our DNA. But DNA affects much more than how we look.

Some genes control when our cells grow, divide into new cells, and die at the right time. Certain genes that help cells grow, divide, or stay alive are called *oncogene*s. Others that slow down cell division or cause cells to die at the right time are called *tumor suppressor*

genes. Cancers can be caused by DNA changes that turn on oncogenes or turn off tumor suppressor genes.

The most important gene in retinoblastoma is the *RB1* tumor suppressor gene. This gene makes a protein (pRb) that helps stop cells from growing too quickly. Each cell normally has 2 *RB1* genes. As long as a retinal cell has at least one *RB1* gene that works as it should, it will not form a retinoblastoma. But when both of the *RB1* genes are mutated or missing, a cell can grow unchecked. This can lead to further gene changes, which in turn may cause cells to become cancerous.

Hereditary or bilateral retinoblastoma

About 1 out of 3 children with retinoblastoma have a germline mutation in one *RB1* gene; that is, all the cells in the body have a defective *RB1* gene. In most of these children (75%), this mutation developed after conception while in the womb. The other 25% of children have inherited it from one of their parents.

About 9 of 10 children who are born with this *RB1* germline mutation develop retinoblastoma. This happens when the second *RB1* gene is lost or mutated. Most often the retinoblastoma is bilateral (in both eyes), but sometimes it is found early enough that it is still only in one eye.

These children have hereditary retinoblastoma. All bilateral retinoblastomas are considered hereditary, although not all hereditary retinoblastomas are bilateral when they are found.

Every person has 2 *RB1* genes but passes only 1 on to each of their children. (The child gets the other *RB1* gene from the other parent.) Therefore there is a 1 in 2 chance that a parent who had hereditary retinoblastoma will pass the mutated gene on to his or her child.

Most children with hereditary retinoblastoma don’t have an affected parent. But these children can still pass their *RB1* gene mutation on to their children. This is why we call this form of retinoblastoma “hereditary” (even though neither of the child’s parents may have been affected).

Non-hereditary (sporadic) retinoblastoma

Most of the remaining 2 out of 3 children with retinoblastoma do not have the *RB1* gene mutation in all the cells of their body. Instead, the *RB1* mutation happens early in life and first occurs only in one cell in one eye.

Whether the changes in the *RB1* gene are hereditary or sporadic, it’s not clear what causes these changes. They may result from random gene errors that sometimes occur when cells divide to make new cells. There are no known lifestyle-related or environmental causes of retinoblastoma, so it’s important to remember that there is nothing these children or their parents could have done to prevent these cancers.

Can retinoblastoma be prevented?

In adults, the risk for many cancers can be reduced by avoiding certain risk factors, such as smoking or exposure to hazardous chemicals in the workplace. But there are no known avoidable risk factors for retinoblastoma. If your child does develop retinoblastoma, it's important to realize that you or your child did nothing to cause it.

In some cases, gene changes that put a person at high risk of retinoblastoma are hereditary (passed on from a parent to a child). People who have had retinoblastoma might want to consider genetic counseling before having children to learn more about the risks of passing on the gene change and perhaps to explore ways to avoid this. For example, an option some people might consider would be to use in vitro fertilization and implant only embryos that don't have the gene change.

If a preventive option is not used, children born to a parent with a history of retinoblastoma should be screened for this cancer starting shortly after birth because early detection of this cancer greatly improves the chance for successful treatment. See the section "Can retinoblastoma be found early?" for more information.

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?”

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*. (Doctors 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.

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.

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 the section "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.

International Classification for Intraocular Retinoblastoma

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.

How is retinoblastoma treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

General treatment information

Retinoblastoma is rare, so not many doctors other than those in specialty eye hospitals and major children's cancer centers have much experience treating it. Children with retinoblastoma and their families have special needs that can best be met by these children's cancer centers. These centers have teams of specialists who know about retinoblastoma and the unique needs of children with cancer. This gives the child the best chance for recovery and, if possible, keeping their sight.

If your child has retinoblastoma, be sure he or she is treated at a children's cancer center that has expertise in treating children with this rare form of cancer. Ask about the services offered

at your treatment center. Your child's doctor or nurse can tell you what is available to help with any problems you or your child might have.

Children with retinoblastoma are treated by a team of doctors that often includes:

- A **pediatric ophthalmologist**: a doctor who treats eye diseases in children
- An **ocular oncologist**: a doctor (usually an ophthalmologist) who treats cancers of the eye
- A **pediatric oncologist**: a doctor who treats children with cancer
- A **radiation oncologist**: a doctor who treats cancer with radiation therapy

The team might also include other doctors, physician assistants (PAs), nurse practitioners (NPs), nurses, therapists, child psychologists, social workers, genetic counselors, and other professionals. Having a child go through cancer treatment often means meeting lots of specialists and learning about parts of the medical system you probably haven't been exposed to before. For more information, see *Children Diagnosed With Cancer: Understanding the Health Care System*.

Once the cancer is found and the needed tests have been done, the cancer care team will discuss treatment options with you. It's important to discuss all of the options as well as their possible side effects with your child's doctors to help you make an informed decision. For a list of some questions to ask, see the section "What should you ask your child's doctor about retinoblastoma?" Then add your own.

If time permits, it can often be helpful to get a second opinion if you have questions about the recommended plan (or if you just want to confirm this is the best option). This can give you more information and help you feel more confident about the treatment plan you choose. Check with your insurance provider about their policy on second opinions.

Treatment principles

The goals of treatment for retinoblastoma are:

- To get rid of the cancer and save the child's life
- To save the eye if possible
- To preserve as much vision as possible
- To limit the risk of second cancers later in life, which can be caused by treatment, particularly in children with hereditary retinoblastoma

The most important factors that help determine treatment are:

- Whether the tumor is just in one eye or both

- How good the vision in the eye is
- Whether the tumor has extended outside the eye

Overall, more than 9 in 10 children with retinoblastoma are cured. The chances of long-term survival are much better if the tumor has not spread outside the eye.

The main types of treatment for retinoblastoma are:

- Surgery
- Radiation therapy
- Photocoagulation (using lasers to kill small tumors or the blood vessels that feed them)
- Cryotherapy (using cold to freeze and kill small tumors)
- Thermotherapy (using a type of laser to apply heat to kill small tumors)
- Chemotherapy
- High-dose chemotherapy and stem cell transplant

Sometimes more than one type of treatment may be used. The treatment options are based on the extent of the cancer and other factors.

Surgery (enucleation) for retinoblastoma

Surgery is not needed for all retinoblastomas, especially for smaller tumors. But if a tumor gets quite large before it is found, vision in the eye has often already been destroyed, with no hope of getting it back. The usual treatment in this case is *enucleation*, an operation to remove the whole eye, plus part of the optic nerve attached to it. This is done while the child is under general anesthesia (in a deep sleep).

During the same operation, an orbital implant is usually put in to take the place of the eyeball. The implant is made out of silicone or hydroxyapatite (a substance similar to bone). It is attached to the muscles that moved the eye, so it should move the same way as the eye would have.

Your child will probably be able to leave the hospital the same day or the next day.

After several weeks, you can visit an *ocularist*, who will create an artificial eye for your child. This is a thin shell that fits over the orbital implant and under the eyelids, like a big contact lens. It will match the size and color of the remaining eye. Once it is in place, it will be very hard to tell it apart from the real eye.

When retinoblastoma occurs in both eyes, enucleation of both eyes would result in complete blindness. If neither eye has useful vision because of damage already caused by the cancer,

this is the best way to make sure all of the cancer is gone. But if there is any chance of saving useful vision in one or both eyes, doctors may advise trying other types of treatment first.

Possible side effects: The most obvious side effect of enucleation is the loss of vision in that eye, although most often the vision has already been lost because of the cancer.

Removing the eye also can affect the future growth of bone and other tissues around the eye socket, which can make the area look somewhat sunken. Using an orbital implant can sometimes lessen this effect. (Radiation therapy, the other major treatment option in such cases, may cause the same side effect.)

Radiation therapy for retinoblastoma

This treatment uses high energy x-rays or particles to kill cancer cells. Radiation therapy is an effective treatment for some children with retinoblastoma. Compared with surgery, it has the advantage of possibly saving vision in the eye. But radiation therapy also has some disadvantages (see “Possible side effects” below).

Two types of radiation therapy can be used to treat children with retinoblastoma.

External beam radiation therapy

External beam radiation therapy (EBRT) focuses radiation beams from a source outside the body on the cancer. This was once a common treatment for retinoblastoma. But because of the side effects it can cause, it is now most often used only for cancers that are not well-controlled with other treatments.

Radiation is usually given 5 days a week for several weeks. Before treatments start, the radiation team takes careful measurements with imaging tests such as MRI scans to determine the correct angles for aiming the radiation beams and the proper dose of radiation.

Each treatment is much like getting an x-ray, but the dose of radiation is much higher. For each session, your child will lie on a special table while a machine delivers the radiation from precise angles.

The actual treatment each day lasts only a few minutes, but the setup time – getting your child into place for treatment – usually takes longer. The child’s head is positioned in a custom-fitted mold that is similar to a cast used to treat broken bones. The treatment is not painful, but young children may be given medicine to make them sleep so they will stay still during treatment.

Newer forms of radiation therapy

Many centers now use newer types of external radiation therapy, which can target the tumor more precisely. This lowers the doses that surrounding normal tissues get, which may help reduce side effects.

Intensity modulated radiation therapy (IMRT): IMRT lets doctors shape the radiation beams and aim them at the tumor from several angles, as well as adjust the intensity (strength) of the beams to limit the dose reaching the nearby normal tissues. This may let the doctor deliver a higher dose to the tumor, while reducing side effects. Many major hospitals and cancer centers now use IMRT.

Proton beam therapy: Protons are positive parts of atoms. Unlike the x-rays used in standard radiation, which release energy both before and after they hit their target, protons cause little damage to tissues they pass through and then release their energy after traveling a certain distance. Proton beam radiation may be able to deliver the same level of radiation to the tumor while causing much less damage to nearby normal tissues. Early results with proton beam therapy are promising, but it's still fairly new, and there is very little long-term data on its use for retinoblastoma. There are only about 15 centers that do proton beam therapy in the United States at this time.

Possible side effects of EBRT

Some of the side effects of EBRT will go away after a short while and are usually not serious. Short-term problems might include effects on skin areas that receive radiation, which can range from mild sunburn-like changes and hair loss to more severe skin reactions.

More importantly, EBRT can damage nearby normal body tissues. This might eventually lead to cataracts (clouding of the lens of the eye) and damage to the retina or optic nerve, which could reduce vision. Radiation can also slow the growth of bones and other tissues near the eye, which can affect the way the area around the eye looks over time.

External radiation therapy can also increase the risk of developing a second cancer in the area. This is especially important in children with the hereditary form of retinoblastoma, who are already at increased risk for developing other types of cancer.

Newer forms of radiation therapy, such as IMRT and proton beam therapy, target the tumor more precisely and spare more normal tissue. This may make some of these side effects less likely than in the past.

Brachytherapy (plaque radiotherapy)

The use of brachytherapy, also known as *internal radiation therapy* or *episcleral plaque radiotherapy*, is limited to small tumors. During brachytherapy, a small amount of radioactive material is placed on the outside of the part of the eyeball where the tumor is for several days. The radioactive material is put in a small carrier (known as a *plaque*), which is shaped like a very small bottle cap. The plaque is made of gold or lead to shield nearby tissues from the radiation. The radiation travels a very short distance, so most of it will be focused only on the tumor.

The plaque is sewn in place on the eyeball with tiny stitches during a short operation. It is then removed during a second operation several days later. Both operations are done while

the child is under general anesthesia (in a deep sleep). The child typically stays in the hospital while the plaque is in place.

Possible side effects: Brachytherapy is less likely to cause side effects than external radiation. The main concern is damage to the retina or optic nerve, which can affect vision many months later. Recent advances in treatment may make this problem less likely. Brachytherapy has not been linked to an increased risk of developing a second cancer.

For more information on radiation therapy, see *Understanding Radiation Therapy: A Guide for Patients and Families*.

Laser therapy (photocoagulation) for retinoblastoma

Photocoagulation is a type of treatment that uses a laser beam aimed through the pupil. The laser is focused on the blood vessels that surround and supply the tumor, destroying them with the heat caused by the beam. Photocoagulation is effective only for smaller tumors toward the back of the eye.

Your child will be under general anesthesia (in a deep sleep) during the treatment. The treatment is usually given 2 or 3 times, with about a month between treatments.

Possible side effects: In some cases, laser therapy can damage the retina, which can lead to blind spots or temporarily cause the retina to detach from the back of the eyeball.

Cryotherapy for retinoblastoma

In cryotherapy, the doctor uses a small metal probe that is cooled to very low temperatures, killing the retinoblastoma cells by freezing them. It is only effective for small tumors toward the front of the eye. It is not used routinely for children with several tumors.

The child will be under general anesthesia (in a deep sleep) during the treatment. After the child is asleep, the probe is placed on the outer surface of the eyeball next to the tumor, which is then frozen and thawed several times. Cryotherapy is usually given 2 or 3 times, with about a month between treatments.

Possible side effects: Cryotherapy can cause the eye and eyelid to swell for a few days. As with laser therapy, cryotherapy can damage the retina, which can lead to blind spots or temporarily cause the retina to detach from the back of the eyeball.

Thermotherapy for retinoblastoma

For thermotherapy (also called *transpupillary thermal therapy*, or TTT), the doctor uses a different type of laser than that used in photocoagulation therapy. The laser applies infrared light to heat and kill the tumor cells. The temperatures are not quite as high as those used in photocoagulation therapy, so some of the blood vessels on the retina may be spared.

Thermotherapy can be used alone for very small tumors. For larger tumors, it can be used along with chemotherapy (called *thermochemotherapy*) or with radiation therapy (called *thermoradiotherapy*). Heat seems to help these other treatments work better.

The treatment is given while the child is asleep, usually for about 10 minutes at a time. Typically, 3 treatments about a month apart are needed to control each tumor. When used as part of thermochemotherapy, the heat is usually applied at a lower temperature over a slightly longer period of time, starting within a few hours after chemotherapy.

Possible side effects: Thermotherapy can sometimes cause part of the iris (the colored part of the eye) to shrink. Other possible effects include clouding of part of the eye lens or damage to the retina, which might affect vision.

Chemotherapy for retinoblastoma

Chemotherapy (chemo) is the use of anti-cancer drugs to treat retinoblastoma.

Ways of giving chemotherapy

Chemo can be given in different ways.

Systemic chemotherapy: In most cases, chemo drugs are injected into a vein (IV) or given by mouth. These drugs enter the bloodstream and reach throughout the body. This is known as *systemic chemotherapy*.

Periocular (subtenon) chemotherapy: For some advanced intraocular cancers, higher doses of chemo are needed inside the eye. Along with systemic chemotherapy, one of the drugs (carboplatin) may be injected in the tissues around the eye, where it slowly diffuses into the eyeball. This is called *periocular* or *subtenon chemotherapy*. These injections are done while the child is under anesthesia (asleep). This can cause redness and swelling around the eye.

Intra-arterial chemotherapy: A newer approach sometimes used instead of systemic chemotherapy is to inject chemo directly into the ophthalmic artery, the main artery that supplies blood to the eye. In this technique, a very thin catheter (a long, hollow, flexible tube) is inserted into a large artery on the inner thigh and slowly threaded through the blood vessels all the way up into the ophthalmic artery. (This is done with the child asleep under general anesthesia.) The chemo is then infused into the artery. The drug used most often is melphalan, but other drugs such as carboplatin and topotecan can also be used. This process may then be repeated every few weeks, depending on how much the tumor shrinks.

Because the chemo is put directly into the artery feeding the eye, doctors can use much smaller doses of chemo drugs (less than 10% of the doses used for systemic chemo). Therefore, there are fewer side effects from the chemo.

Early results with this technique in eyes with advanced tumors have been promising, generally with good tumor control and few side effects. In most cases it has allowed doctors to save an eye that otherwise would have needed to be removed.

Intravitreal chemotherapy: In this newer approach, chemotherapy is given directly into the vitreous humor, the jelly-like substance inside the eye. This approach is discussed in the section "What's new in retinoblastoma research and treatment?"

Uses of chemotherapy

Chemotherapy may be used in different situations:

- Chemo can be used as the first treatment to shrink some tumors that have not spread outside the eye. This is called *chemoreduction*. These tumors can then be treated more effectively with focal therapies such as laser therapy, cryotherapy, thermotherapy, or brachytherapy.
- Systemic (IV) chemo may be given to children whose tumors don't seem to have spread beyond the eye, but might be likely to spread because of the tumor's size and/or location.
- Chemo is sometimes used when the eye has already been removed, but the tumor was found to extend into some areas in the eye that make it more likely to have spread. This type of treatment is called *adjuvant chemotherapy*.
- Systemic chemo is also used to treat children whose retinoblastoma has spread beyond the eye, a much more critical situation. If the cancer has spread to the brain, chemo may also be given directly into the cerebrospinal fluid that surrounds it (known as *intrathecal chemotherapy*). Tumors outside the eye may shrink for a time with standard doses of chemo, but they will usually start growing again. For this reason, doctors often prefer to give more intense chemo, usually along with a stem cell transplant. (See the section "High-dose chemotherapy and stem cell transplant.")

Doctors give systemic chemo in cycles, with each period of treatment followed by a rest period to give the body time to recover. Each chemo cycle typically lasts for a few weeks, and the total length of treatment is often several months.

Some of the drugs used to treat children with retinoblastoma include:

- Carboplatin
- Cisplatin
- Vincristine
- Etoposide
- Cyclophosphamide

- Topotecan
- Doxorubicin

Most often, 2 or 3 drugs are given at the same time. A standard combination used to shrink intraocular retinoblastomas is carboplatin, vincristine, and etoposide, although for very small tumors, only carboplatin and vincristine may be enough. Other drugs might be used if these are not effective.

Possible side effects

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow (where new blood cells are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemo, which can lead to side effects.

Children tend to have less severe side effects from chemo and to recover from side effects more quickly than adults do. One benefit of this is that doctors can give them the high doses of chemo needed to kill the tumor.

The side effects of chemo depend on the type of drugs, the doses used, and how long they are given. Possible short-term side effects include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea or constipation
- Increased chance of infections (from having too few white blood cells)
- Easy bruising or bleeding (from having too few blood platelets)
- Fatigue (from having too few red blood cells)

Most of these side effects go away after treatment is finished. There are often ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting. Be sure to discuss any questions about side effects with your child’s cancer care team, and let them know if your child has side effects so they can be managed.

Along with those listed above, certain chemo drugs can cause specific side effects. For example:

- Cisplatin and carboplatin can affect the kidneys. Giving the child plenty of fluids during treatment can help reduce this risk. These drugs can also cause hearing loss in young children, especially in babies younger than 6 months. Your child's doctor may check your child's hearing with tests during or after treatment. When carboplatin is injected directly into the tissues near the eye (periocular chemotherapy), it can cause redness and swelling in the area.
- Vincristine can damage nerves. Some children may feel tingling and numbness, particularly in their hands and feet.
- Some drugs, such as etoposide, doxorubicin, and cyclophosphamide, can increase the risk of developing a cancer of white blood cells known as *acute myeloid leukemia* (AML) later in life. Fortunately, this is not common.
- Doxorubicin can damage the heart. The risk of this happening goes up with the total amount of the drug given. Doctors try to limit this risk as much as possible by not giving more than the recommended doses and by checking the heart with an echocardiogram (an ultrasound of the heart) during treatment.
- Cyclophosphamide can damage the bladder, which can cause blood in the urine. This risk can be lowered by giving this drug along with plenty of fluids and with a drug called mesna, which helps protect the bladder.

For more information about chemotherapy, see *A Guide to Chemotherapy*.

High-dose chemotherapy and stem cell transplant for retinoblastoma

Doctors are studying the use of this type of treatment in children with retinoblastoma that has spread outside the eye and who are unlikely to be cured with other treatments.

A stem cell transplant (SCT) lets doctors give higher doses of chemotherapy (chemo) than could safely be given otherwise). In the past, this type of treatment was commonly referred to as a *bone marrow transplant*.

The bone marrow is the soft, inner part of some bones where new blood cells are made. Chemo drugs can affect quickly dividing cells like those in the bone marrow. 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.

How is it done?

The first step in a SCT is to collect, or harvest, the child's own blood-making stem cells to use later. (These are the cells that make the different types of blood cells.)

In the past, the stem cells were often taken from the child's bone marrow, which required a minor operation. But doctors have found that these cells can be taken from the bloodstream during a procedure similar to donating blood. Instead of going into a collecting bag, the blood goes into a special machine that filters out the stem cells and returns the rest of the blood to the child's body. The stem cells are then frozen until the transplant. This process may need to be done more than once.

Once the stem cells have been stored, the child gets high-dose chemotherapy in the hospital, sometimes along with radiation therapy. When the treatment is finished (a few days later), the stem cells are thawed and returned to the body in a process similar to a normal blood transfusion. The stem cells travel through the blood and settle in the bone marrow.

Over the next few weeks, the stem cells start to make new blood cells. Until this happens, the child is at high risk of infection because of a low white blood cell count, as well as bleeding because of a low platelet count. To avoid infection, protective measures are taken, such as using special air filters in the hospital room and having visitors wear protective clothing. Blood and platelet transfusions and treatment with IV antibiotics may also be used to prevent or treat infections or bleeding problems.

The child can usually leave the hospital once their blood cell counts return to a safe level. They may then need to make regular visits to the outpatient clinic for about 6 months, after which time their care may be continued by their regular doctors.

Practical points

A SCT is a complex treatment that can cause life-threatening side effects. If the doctors think your child can benefit from a transplant, the best place to have it done is at a nationally recognized cancer center where the staff has experience with the procedure and with managing the recovery period.

A stem cell transplant often requires a long hospital stay and can be very expensive, often costing well over $100,000. Be sure to get a written approval from your insurer before treatment if it is recommended for your child. Even if the transplant is covered by your insurance, your co-pays or other costs could easily amount to many thousands of dollars. It's important to find out what your insurer will cover before the transplant to get an idea of what you might have to pay.

Possible side effects

The possible side effects from SCT are generally divided into early and long-term effects.

Short-term, early side effects: The early complications and side effects are basically the same as those listed in the “Chemotherapy” section, but they can be more severe because the drug doses are higher. Side effects can include:

- Low blood cell counts (with fatigue and an increased risk of infection and bleeding)
- Nausea and vomiting
- Loss of appetite
- Mouth sores
- Diarrhea
- Hair loss

One of the most common and serious short-term effects is an increased risk of serious infections. Antibiotics are often given to try to keep this from happening. Other side effects, like low red blood cell and platelet counts, may require blood product transfusions or other treatments.

Long-term and late side effects: Some complications and side effects can last for a long time or might not occur until months or years after the transplant. These can include:

- Radiation damage to the lungs
- Problems with the thyroid or other hormone-making glands
- Problems with fertility
- Damage to bones or problems with bone growth
- Development of another cancer (including leukemia) years later

Be sure to talk to your child’s doctor before the transplant to learn about possible long-term effects your child might have. For more on the long-term effects of this and other treatments, see the section “Late and long-term effects of treatment for retinoblastoma.”

To learn more about stem cell transplants, see *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants).*

Clinical trials for retinoblastoma

You may have had to make a lot of decisions since you’ve been told your child has retinoblastoma. One of the most important decisions you will make is deciding which treatment is best. You might have heard about clinical trials being done for this type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. These studies are done to learn more about promising new treatments or procedures.

Clinical trials are one way to get state-of-the-art cancer care for your child. Sometimes they may be the only way to get access to some newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they might not be right for every child.

If you would like to learn more about clinical trials your child may be eligible for, start by asking your doctor if your clinic or hospital conducts clinical trials. Children's cancer centers often conduct many clinical trials at any one time, and in fact most children treated at these centers take part in a clinical trial as part of their treatment.

You can also call our clinical trials matching service for a list of studies that might meet your child's needs. You can reach this service at 1-800-303-5691 or on our website at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute (NCI) at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials website at www.cancer.gov/clinicaltrials.

Your child will have to meet certain requirements to take part in any clinical trial. If your child does qualify for a clinical trial, you will have to decide whether or not to enter (enroll) the child into it.

To learn more about clinical trials, see *Clinical Trials: What You Need to Know*.

Complementary and alternative therapies for retinoblastoma

You might hear about ways to treat your child's cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to social media groups and websites may offer ideas for what might help. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help the person with cancer feel better. Some methods that are used along with regular treatment are: art therapy or play therapy to reduce stress; acupuncture to help relieve pain; or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few have even been found to be harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may be dangerous, or have life-threatening side effects. But the biggest danger in most cases is that your child could lose the chance to be helped by standard medical treatment. Delaying or interrupting medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It's easy to see why parents who have children with cancer think about alternative methods. You want to do all you can to help fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most alternative methods have not been tested and proven to work in treating cancer.

As you consider your child's options, look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country? Also be sure to talk to your child's cancer care team about any method you are thinking about using.

You can find more tips on what to look for and how to make these decisions in the "Complementary and Alternative Medicine" section of our website.

The choice is yours

You always have a say in how your child is treated. If you want to use a non-standard treatment, learn all you can about the method and talk to your child's doctor about it. With good information and the support of your child's health care team, you may be able to safely use the methods that can help your child while avoiding those that could be harmful.

Treatment of retinoblastoma, based on extent of the disease

If your child has retinoblastoma, a number of factors can affect the treatment options your child's doctor recommends. Some of these include:

- Whether tumors are in one or both eyes
- The size and location of the tumor in the eye(s)
- The chance for saving vision in the eye(s)
- Whether the tumor is still confined within the eye(s) or has spread elsewhere

If the retinoblastoma is only in one eye, treatment depends on whether vision in the eye can be saved. If the chance to save vision is poor, the treatment is often surgery to remove the

eye. Surgery was used more often in the past even for smaller tumors, as it offered the best chance to ensure all of the cancer was removed. But in recent years, doctors have become more comfortable with using other treatments (often intra-arterial chemotherapy plus some form of local treatment) if there is a good chance of saving vision in the eye.

If the retinoblastoma is in both eyes, doctors will try to save at least one eye if at all possible so that the child maintains some vision. Most children with retinoblastoma in both eyes will be treated with chemotherapy (intra-arterial or systemic) first to shrink the tumors (called *chemoreduction*), followed by some form of local treatment and possibly radiation therapy. Surgery (removal of the eye) is reserved for the most advanced tumors and for those that do not respond to chemoreduction and local treatments.

Many children will get several types of treatment. Treatment might be needed for months or even years, especially in eyes treated with cryotherapy and/or photocoagulation after chemotherapy.

No matter which types of treatment are used, it’s very important that they are given by experts at centers experienced in treating these tumors.

If the eye can see and probably can be saved

For some smaller tumors, local treatments such as laser therapy (photocoagulation) or cryotherapy may be the only treatment needed.

More often, tumors are larger or in hard-to-treat areas. Treatment usually includes a combination of chemotherapy and focal treatments. If systemic chemotherapy (chemotherapy given by vein) is used, it is given for about 6 months to shrink the tumor as much as possible. More recently, many centers have begun to give chemotherapy directly into the artery that feeds the eye (known as *intra-arterial chemotherapy*) instead of systemic chemotherapy. Usually a few treatments are needed, each given a few weeks apart.

Depending on how much the tumor shrinks and where it is in the eye, different focal treatments can then be applied, usually starting after the first or second cycle of chemotherapy. Treatment options may include brachytherapy (plaque radiotherapy), cryotherapy, laser therapy (photocoagulation), or thermotherapy. External radiation therapy may also be given, but it is usually delayed until the end of chemotherapy.

If the combination of these treatments doesn’t control the disease, surgery to remove the eye may be needed.

If the eye cannot see or cannot be saved

If there is no vision in the eye, if the tumor is so advanced within the eye that there is no hope of cure by other means, or if there is painful glaucoma, then surgery is done to remove the eye and place an orbital implant in the socket.

If the cancer affects only one eye, no other treatments may be required. But sometimes, after looking at the removed eye under the microscope, the doctors find that some retinoblastoma cells might have escaped the eye and thus may come back later in other parts of the body. These children may be given chemotherapy, possibly along with radiation therapy to the area around the eye, to try to lower this risk.

In some instances where there are large tumors in both eyes, chemotherapy may be used first to try to shrink the tumors and avoid the need for surgery in both eyes. If chemotherapy shrinks the tumors enough, local therapies such as brachytherapy (plaque radiotherapy), cryotherapy, laser therapy (photocoagulation), or thermotherapy might allow at least one eye (and some vision) to be saved.

Some children with retinoblastoma in only one eye may actually have the hereditary form of retinoblastoma, which means they will probably develop disease in the other eye as well. Therefore, it is very important that children with retinoblastoma in one eye continue to have the other eye examined regularly after treatment.

If the cancer has spread outside the eye

In this uncommon situation, treatment is usually a combination of chemotherapy, radiation, and in some cases surgery.

If the cancer has spread only to the orbit (the area around the eye), treatment with chemotherapy, surgical removal (enucleation) of the eye, and radiation therapy to the orbit is often successful.

If the cancer has spread outside the orbit to distant parts of the body such as the liver or the bones and bone marrow, the chances of a cure using standard chemotherapy and other treatments are very low. In these cases, using higher doses of chemotherapy followed by a stem cell transplant can often be successful.

Cancers that have spread to the brain (including trilateral retinoblastomas, which are retinoblastomas that usually start in the pineal gland) are very hard to treat, and the chances of a cure using standard treatments are low. High-dose chemotherapy and stem cell transplant has shown some promise for these cancers in a recent small study. Clinical trials using other newer treatments may be an option in this situation as well.

If the cancer comes back in the eye after initial treatment

Treatment of cancer that recurs in the eye depends on the size and location of the tumor and on what treatments were used the first time. If the tumor is small, the child’s sight can often be saved while the cancer is destroyed with local treatments such as cryotherapy, laser therapy, radiation therapy (if not already used), or other treatments. Chemotherapy may be given first. If the child’s sight cannot be saved, the eye may need to be removed with surgery. Either way, the chance of a cure is very good as long as the cancer is still confined to the eye.

If the cancer comes back outside the eye after initial treatment

Cancers that recur outside the eye are harder to treat. Options may include chemotherapy and radiation, or high-dose chemotherapy with a stem cell transplant in some cases. In this situation, the treatment and the chances of cure are similar to what is described above (when the cancer has spread outside the eye before initial treatment).

Summary

If the cancer is in only one eye and the potential for saving sight is good, chemotherapy (either by vein or directly into the artery of the eye) and local treatments such as cryotherapy laser therapy (photocoagulation), thermotherapy, or plaque radiation are used (although very small tumors, which are very rare, can be treated with local treatments alone). Otherwise the eye will likely need to be removed.

If the cancer is in both eyes, then the doctors will try to save as much vision as possible. The treatment usually starts with chemotherapy, followed by local treatments.

In all cases, children who have had retinoblastoma need to be followed closely for some time after treatment.

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 *Talking With Your Doctor*.

What happens after treatment for retinoblastoma?

During and after treatment for retinoblastoma, the main concerns for most families are the short- and long-term effects of the cancer and its treatment, and concerns about the cancer still being there or coming back.

It’s certainly normal to want to put the tumor and its treatment behind you and to get back to a life that doesn’t revolve around cancer. But it’s important to realize that follow-up care is a central part of this process that offers your child the best chance for recovery and long-term survival.

Follow-up exams and tests

Once treatment is finished, your health care team will discuss a follow-up schedule with you, including which tests should be done and how often. It’s very important to go to all follow-up appointments. Follow-up is needed to check for cancer recurrence, as well as possible side effects of certain treatments. Doctor visits and tests are done more often at first. If nothing abnormal is found, the time between tests can then be extended.

If a child with retinoblastoma in only one eye has been treated by enucleation (removal of the eye), regular exams are needed to look for tumor recurrence or spread, or any growth problems related to the surgery. It’s also important to have the remaining eye checked regularly so that if a second retinoblastoma develops later on it can be found and treated as early as possible.

For children who have had treatment other than removal of the eye, close follow-up exams by an ophthalmologist (eye doctor) are very important to look for signs of the cancer coming back or other problems. In children with hereditary retinoblastoma, it’s very common for new tumors to form until they are 3 or 4 years old. This is not a failure of the treatment, but the natural process in bilateral retinoblastoma. Therefore, it’s very important that even after completing all treatments, children are examined regularly by specialists.

During these exams, general anesthesia (where the child is asleep) may be needed to keep a young child still enough for the doctor to do a thorough eye exam. This is done to be certain the cancer has been destroyed, to find recurrences as early as possible, and to look for problems caused by treatments.

It’s important for you to report any new symptoms your child is having, such as pain or vision problems, to your doctor right away, since they could be an early sign of cancer coming back or long-term side effects of treatment.

Keeping good medical records after treatment for retinoblastoma

As much as you might want to put the experience behind you once treatment is done, it’s very important to keep good records of your child’s medical care during this time. This can be very helpful for your child later on as an adult and for his or her doctors. Gathering these details during or soon after treatment may be easier than trying to get them at some point in the future. Be sure your child’s doctors have the following information (and always keep copies for yourself):

- A copy of the pathology report(s) from any biopsies or surgeries
- If your child had surgery, a copy of the operative report(s)
- If your child stayed in the hospital, copies of the discharge summaries that the doctors wrote when he or she was sent home
- If chemotherapy was given, a list of the drugs, drug doses, and when they were given
- If radiation therapy was given, a summary of the type and dose of radiation and when and where it was given
- If genetic testing was done, the results of those tests
- The names and contact information of the doctors who treated your child's cancer

It's also very important to keep health insurance coverage. Tests and doctor visits cost a lot, and even though no one wants to think of the cancer coming back, this could happen.

Genetic counseling and testing for retinoblastoma

If you have a child with retinoblastoma, your doctor may suggest your family consider genetic counseling. This is because some retinoblastomas are caused by a genetic mutation that can be inherited.

If a child is diagnosed with retinoblastoma in both eyes, it can be assumed that they have the hereditary form of the disease (even if there is no family history of the disease), which means they carry the mutant *RB1* gene in all their cells. Some children with retinoblastoma in only one eye might also carry the mutant *RB1* gene in all their cells. This can be confirmed with a blood test. Children with this mutant gene are at increased risk for developing other cancers later in life (see the section "Second cancers"), and will have a 1 in 2 chance of passing the *RB1* gene change on to each of their children.

If the child carries the mutated *RB1* gene, then other children in the family might have inherited the same abnormal gene as well. Meeting with a genetic counselor can give you a better idea of what this risk might be and if other children in the family should be tested for the mutation. The genetic counselor will:

- Review the child's medical records and ask questions about other relatives to estimate the likelihood of an inherited gene affecting some family members.
- Provide information and answer questions about genetic testing, and schedule tests for other children in your family (if needed) to help determine their risk of developing retinoblastoma.

If tests show your children are at risk of developing retinoblastoma, their doctors will follow them very closely to find retinoblastoma at the earliest possible stage, if it occurs. It's very

helpful to be able to tell which children have inherited the mutation that leads to retinoblastoma, since those children will need to be monitored closely.

Sometimes it's not possible to tell with certainty if a child inherited the *RB1* gene mutation. In those cases the safest plan is to monitor children in the family closely for retinoblastoma with frequent eye exams.

Late and long-term effects of treatment for retinoblastoma

With major advances in treatment in recent decades, most children treated for retinoblastoma are now expected to have normal lifespans. But some of the treatments needed to cure the cancer can affect children's health later in life, so watching for health effects as they get older has become more of a concern in recent years.

Just as the treatment of childhood cancer requires a very specialized approach, so does the care and follow-up after treatment. The earlier any problems can be recognized, the more likely it is they can be treated effectively.

Young people treated for retinoblastoma are at risk, to some degree, for several possible late effects of their cancer treatment. It's important to discuss what these possible effects might be with your child's medical team.

The risk of late effects depends on a number of factors, such as the specific treatments used, the doses of treatment, and the age of the child when being treated. These late effects can include:

- Reduction or loss of vision in the affected eye(s)
- Deformities in the bones around the eye (especially after surgery or external radiation)
- Reduced kidney function
- Heart problems after getting certain chemotherapy drugs
- Slowed or delayed growth and development
- Changes in sexual development and ability to have children (see *Fertility and Women With Cancer* and *Fertility and Men With Cancer*)
- Increased risk of other cancers (especially in children with hereditary retinoblastoma – see the section "Second cancers")

Other complications from treatment are possible as well. Your child's doctor should carefully review any possible problems with you.

Long-term follow-up care

To help increase awareness of late effects and improve follow-up care of childhood cancer survivors throughout their lives, the Children's Oncology Group (COG) has developed long-term follow-up guidelines for survivors of childhood cancers. These guidelines can help you know what to watch for, what type of screening tests should be done to look for problems, and how late effects can be treated.

It's very important to discuss possible long-term complications with your child's health care team, and to make sure there is a plan in place to watch for these problems and treat them, if needed. To learn more, ask your child's doctors about the COG survivor guidelines. You can also read them on the COG website: www.survivorshipguidelines.org. The guidelines are written for health care professionals. Patient versions of some of the guidelines are available (as "Health Links") on the site as well, but we urge you to discuss them with your doctor.

For more about some of the possible long-term effects of treatment, see *Children Diagnosed With Cancer: Late Effects of Cancer Treatment*.

Second cancers after retinoblastoma

Hereditary retinoblastoma

Children with the hereditary form of retinoblastoma have a much higher risk for developing other types of cancer throughout their lives. This is because each cell in the body has an abnormal *RB1* tumor suppressor gene, which would normally help stop some of these cancers from forming.

The risk for these cancers is even higher in any parts of the body that received radiation during treatment for retinoblastoma. Younger children treated with radiation therapy are more likely than older children to develop side effects such as second cancers or problems with bone growth in the irradiated area. Chemotherapy with certain drugs can also increase the risk of some cancers.

Most of these cancers are very treatable if detected early, which is why it is very important that these children are followed closely throughout life. The entire body must be examined carefully to avoid missing these second cancers.

The most common second cancers among retinoblastoma survivors include:

- Osteosarcoma (a type of bone cancer)
- Soft tissue sarcomas (cancers that develop in muscle, tendons and ligaments, and fatty tissue)
- Melanoma (a type of skin cancer)

- Lung cancer
- Lymphoma
- Bladder cancer
- Uterine cancer
- Breast cancer
- Brain tumors
- Cancers in the mouth or nose

HYPERLINK "http://www.cancer.org/redirect/index?friendlyURL=retinoblastoma-treating-radiation-therapy"Because of the increased risk these children face, it’s important that they’re taught about other factors that might increase their risk of cancer as they get older. For example, too much sun exposure can increase the risk of melanoma even further, and smoking can increase lung cancer risk, so avoiding these types of risk factors is very important. It’s also important to know what types of cancer screening tests these children might need as they get older. Of course, these children are also at risk of other cancers as they get older, just like children who did not have retinoblastoma.

Children with hereditary retinoblastoma also have a small risk of developing a tumor in the pineal gland within a few years. (This is known as *trilateral retinoblastoma*.) The pineal gland is a bean-sized structure lying under the middle of the brain. It can have cells similar to retina cells, which is why tumors can start there. This is why doctors often recommend that MRI scans of the head be done regularly for up to 5 years to try to detect such tumors as early as possible.

Non-hereditary (sporadic) retinoblastoma

Children who do *not* have the hereditary form of retinoblastoma don’t have the *RB1* gene change in all of their cells, so they don’t have such a high risk of other cancers. Still, their risk of some cancers might be higher from getting chemotherapy and/or radiation therapy. These children are also at risk for other cancers as they get older, just like children who did not have retinoblastoma.

Emotional and social issues for children with retinoblastoma and their families

Most children with retinoblastoma are very young at the time of diagnosis. Still, some children may have emotional or psychological issues that need to be addressed during and after treatment. Depending on their age, they may also have some problems with normal functioning and school work. These can often be overcome with support and encouragement.

Doctors and other members of the health care team can recommend special support programs and services to help children during and after treatment.

Parents and other family members can also be affected, both emotionally and in other ways. The treatment center should evaluate the family situation as soon as possible. Some common family concerns include financial stresses, traveling to and staying near the cancer center, and the need for family members to take time off from work. If the patient or family members have concerns, they can be addressed before they become a crisis.

Centers that treat many patients with retinoblastoma may have programs to introduce new patients and their families to others who have finished their treatment. This can give parents an idea of what to expect during and after treatment, which is very important. Seeing another patient with retinoblastoma doing well is often helpful.

If needed, centers can also refer patients to special programs and facilities for the visually impaired. Most patients treated for retinoblastoma in only one eye will have normal vision in the unaffected eye, but they may have a cosmetic deformity in the treated eye. The cosmetic problems can often be lessened by treatment in a center with expertise in reconstructive surgery. Early intervention and counseling can also help address any psychological effects of changes in appearance.

Support groups for families of children with cancer can also be helpful. If you need help finding such a group, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you.

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.

Additional resources for retinoblastoma

More information from your American Cancer Society

Here is more information you might find helpful. You also can order free copies of our documents from our toll-free number, 1-800-227-2345, or read them on our website, www.cancer.org

Children with cancer

Health Professionals Associated With Cancer Care

Talking With Your Doctor (also in Spanish)

Children Diagnosed With Cancer: Dealing with Diagnosis (also in Spanish)

Pediatric Cancer Centers (also in Spanish)

Children Diagnosed With Cancer: Understanding the Health Care System (also in Spanish)

Children Diagnosed With Cancer: Financial and Insurance Issues

Children Diagnosed With Cancer: Returning to School

Children Diagnosed With Cancer: Late Effects of Cancer Treatment

Coping with cancer

After Diagnosis: A Guide for Patients and Families (also in Spanish)

Family and Medical Leave Act (FMLA) (also in Spanish)

Nutrition for Children With Cancer (also in Spanish)

What Happened to You, Happened to Me (children's booklet)

When Your Brother or Sister Has Cancer (children's booklet)

When Your Child's Treatment Ends: A Guide for Families (booklet)

Cancer treatment information

A Guide to Cancer Surgery (also in Spanish)

A Guide to Chemotherapy (also in Spanish)

Understanding Radiation Therapy: A Guide for Patients and Families (also in Spanish)

Clinical Trials: What You Need to Know (also in Spanish)

Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants) (also in Spanish)

Side effects from cancer and its treatment

Caring for the Patient with Cancer at Home: A Guide for Patients and Families (also in Spanish)

Nausea and Vomiting

Guide to Controlling Cancer Pain (also in Spanish)

Anemia in People With Cancer

Fatigue in People With Cancer

Fertility and Women With Cancer

Fertility and Men With Cancer

Books

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online at cancer.org/bookstore to find out about costs or to place an order.

National organizations and websites*

Along with the American Cancer Society, other sources of information and support include:

Websites for parents and adults

American Childhood Cancer Organization (formerly Candlelighters)
Toll-free number: 1-855-858-2226
Website: www.acco.org

> Offers information for children and teens with cancer, their siblings, and adults dealing with children with cancer. Also offers books and a special kit for children newly diagnosed with cancer, as well as some local support groups.

Children's Oncology Group (COG)
Website: www.childrensoncologygroup.org

> Provides key information from the world's largest organization devoted to childhood cancer research to help support children and their families from the time of diagnosis, through treatment, and beyond. Also has a searchable database to find the COG center closest to you.

CureSearch for Children's Cancer
Toll-free number: 1-800-458-6223
Website: www.curesearch.org

> Provides up-to-date information about childhood cancer from pediatric cancer experts. Has sections on the website for patients, families, and friends to help guide them on how to support the child with cancer.

National Cancer Institute
Toll-free number: 1-800-4-CANCER (1-800-422-6237)
TTY: 1-800-332-8615
Website: www.cancer.gov

> Provides accurate, up-to-date information about cancer for patients and their families, including clinical trials information. Offers a special booklet for teen siblings of a child with cancer at: www.cancer.gov/cancertopics/when-your-sibling-has-cancer.

National Children's Cancer Society, Inc.
Toll-free number: 1-800-5-FAMILY (1-800-532-6459)
Website: www.children-cancer.org

> Services include an online support network for parents of children with cancer, educational materials, and financial assistance for treatment-related expenses.

Websites for children

Starlight Children's Foundation
Toll-free number: 1-310-479-1212
Website: www.starlight.org

> Website has animated stories and interactive programs to teach kids about chemo and procedures that may be done in the hospital.

SuperSibs! Powered by Alex's Lemonade Stand
Toll-free number: 1-866-333-1213
Website: www.supersibs.org

> Supports, honors, and recognizes brothers and sisters of children diagnosed with cancer so they may face the future with strength, courage, and hope.

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us any time day or night for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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