Retinoblastoma
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Dedicated to the memory of Dr. Charles Pratt, who pioneered treatment for retinoblastoma at St. Jude Children’s Research Hospital from 1970–2002.

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WHAT IS RETINOBLASTOMA?

Retinoblastoma is a cancer of one or both eyes which usually occurs in children who are younger than 5 years of age. The tumor(s) occur in the retina (the innermost layer of the eyeball), which is the area of the eye containing nerves that control vision. Retinoblastoma is the most common intraocular (eye) childhood cancer and has an excellent prognosis, with a greater than 95% cure rate if the disease is contained within the retina when diagnosed. There are 2 forms of retinoblastoma, unilateral (one eye involved) and bilateral (both eyes involved). The majority of patients (60%) have unilateral disease and are diagnosed between 18 and 36 months of age. The remaining 40% of patients have bilateral tumors and are usually diagnosed at a younger age (often during the first year of life and rarely after 2 years of age).

STRUCTURE AND FUNCTION OF THE EYE

It is helpful to know the names, locations, and functions of the structures of the eye to understand your child’s tumor.

The eye has three layers with a total thickness of about ¾-inch (in a child) from front to back:
- Sclera: the white outer covering that protects the eye
- Choroid: the middle layer, which contains the blood vessels that bring nourishment to the eye
- Retina: the inner layer, which contains the nerves that send messages to the brain for sight.

Other structures of the eye include the following:
- Cornea: the clear portion at the front of the eye through which light rays pass
- Conjunctiva: a thin membrane that lines the outside of the eye
- Iris: the colored part of the eye
- Pupil: the black opening in the middle of the iris that allows light into the eye
- Lens: the area behind the iris and pupil that focuses light onto the retina
- Vitreous humor: a gel-filled chamber of the eye that nourishes the eye and gives it shape
- Macula: the part of the retina that provides central vision
- Optic nerve: the nerve that carries messages from the eye to the brain.

WHAT ARE SOME OF THE SYMPTOMS OF RETINOBLASTOMA?

The most common signs of retinoblastoma are leukocoria and strabismus. Leukocoria is often called “cat eye reflex”. It is a white reflection (similar to a cat’s eye in the evening) seen in the pupil (black portion of the eye) when light shines in a child’s eye, instead of a red reflection (a red glow in dim light that is commonly seen in flash pictures). Strabismus is a wandering eye, or abnormal turning in or out of the eye, that does not go away.

Other less common symptoms are changes in vision, eye irritation, and pain. When these symptoms are present, your child also may rub his or her eye frequently or have redness of the eye and tearing, along with vomiting.
WHAT CAUSES RETINOBLASTOMA?
Retinoblastoma is caused by a mutation (mistake) in a gene that can occur sporadically (randomly) or be inherited from a parent.

WHO GETS RETINOBLASTOMA?
Retinoblastoma is a rare form of cancer that occurs once in every 12,000–34,000 live births. It makes up only 1%–3% of all childhood malignancies. Children who have a family history of retinoblastoma have a much greater chance of developing the disease.

IS RETINOBLASTOMA INHERITED?
Retinoblastoma can be inherited but also can occur randomly. Children with bilateral retinoblastoma are born with a genetic change (called a mutation) that causes them to develop retinoblastoma early in life. These children are born with a genetic mutation (gene mistake) that may cause them to develop retinoblastoma during their first few years of life. Only 10% of all children with newly diagnosed bilateral retinoblastoma have a parent with a history of retinoblastoma. These children inherit the mutation from the parent with retinoblastoma. The other 90% do not have a parent with retinoblastoma; they develop the mutation in early development (during pregnancy). The cause of the mistake or mutation is unknown.

The inherited form of retinoblastoma is diagnosed at a younger age and can occur in both eyes or with multiple (more than one) tumors in one eye. Children who have the inherited form of retinoblastoma can pass this cancer on to their own children; there is a 50% chance of retinoblastoma occurring with each pregnancy.

Children who have unilateral (one affected eye) retinoblastoma with a single tumor usually do not have the inherited form. They have a 15% chance of having the inherited form and passing this cancer on to their children. Genetic testing (usually by taking a blood sample) is the only way to know for sure whether a single retinoblastoma tumor is inherited or not. When a child is diagnosed with retinoblastoma, the family usually is referred for genetic counseling. Genetic counselors work as members of a healthcare team, providing information and support to families who have a history of birth defects or genetic disorders and to those who may be at risk for a variety of inherited conditions. They investigate the health problems in the family, interpret information about the disorder, analyze inheritance patterns and risks of recurrence, and review available options with the family. Genetic counselors also provide supportive counseling to families, serve as patient advocates, and refer individuals and families to community or state support services when appropriate.

WHAT ARE METASTASES?
Metastases refer to spread of the tumor from its original location to other parts of the body. Retinoblastoma can metastasize to other parts of the eye, the bones, bone marrow, spinal fluid, or the brain.
WHAT IS STAGING?
Staging is a very important process that is used to identify the location and size of the tumor at the time of diagnosis. For several decades, the Reese-Ellsworth staging system was used as the primary international staging system for retinoblastoma. It was designed to predict the chance of controlling the disease and saving the vision in the affected eye(s). In the late 1990s, a new staging system called the ABCDE system was developed, and it has replaced the Reese-Ellsworth system at most treatment centers. The ABCDE system grades tumors by their size, number, and location in the retina. The advantage of this new system is that it more accurately describes the degree of disease in the eye, helping the treating doctor(s) to better determine the type of therapy needed for each child.

WHICH TESTS AND PROCEDURES WILL MY CHILD NEED?
The following tests may need to be done to evaluate the location and extent of the cancer and determine the most appropriate treatment. All children should receive a magnetic resonance imaging (MRI) or computed tomography (CT) scan of the brain and orbits (eyes), an eye examination under anesthesia (EUA), and possibly an ultrasound of the orbits. Some children who have a higher-stage disease also will need a bone marrow aspirate, bone marrow biopsy, bone scan, and blood tests. Although advanced retinoblastoma is uncommon in the United States and other developed countries, these tests are still needed to ensure that the retinoblastoma has not spread to other parts of the body.

MRI
An MRI is a test that gives very exact pictures of the organs and tumors inside the body. During an MRI test, your child will lie on a table that moves into a tube-like machine surrounding him or her with a magnetic field. The test is painless, but the machine makes quite a bit of noise. Your child must not move at all during the test; therefore, your child will be put to sleep with medicine (IV sedation or general anesthesia) so that he or she will be able to lie completely still during the test. For suspected retinoblastoma, an MRI of the brain and orbits (eyes) is performed. An MRI does not expose your child to any form of radiation.

CT SCAN
The CT scan is a computer-assisted X ray that shows very precise pictures of soft tissues, internal organs, and tumors. The scan is painless, but your child must be able to lie absolutely still during the scan (younger children may require sedation to put them to sleep). A small amount of contrast (dye) is injected into your child's vein to show more detailed pictures. When your child receives the contrast into their vein (via an IV), he or she may have a warm, flushing feeling. Generally, there are no side effects from the contrast, although a small number of children may experience an allergic reaction. Medications are available immediately if an allergic reaction occurs.

EYE EXAM UNDER ANESTHESIA (EUA)
Retinoblastoma is unlike other tumors because a biopsy of the tumor cannot be obtained by surgically removing a piece of it from the eye for examination. Instead, a thorough eye exam under anesthesia (EUA) is performed. During EUA, your child is put into a deep sleep, and the ophthalmologist (eye doctor)
examines the inside of the eye(s) after they are dilated (opened widely) with special eye drops. Retinoblastoma can be diagnosed based on how the tumor(s) look inside the eye. The stage of retinoblastoma is based on the number, size, and location of the tumor(s) that are seen by the ophthalmologist during the EUA. The type and intensity of treatment is based on the stage of the disease.

ULTRASOUND
This test uses high-frequency sound waves to look at internal body organs or tumors. It is painless and involves no radiation. For retinoblastoma, an ultrasound of the orbits (eyes) may be part of the initial diagnostic evaluation.

BONE MARROW TESTS
Bone marrow is the blood-producing factory of the body. To determine if retinoblastoma cells have metastasized (spread) to the bone marrow, a bone marrow aspirate and a bone marrow biopsy may be performed. For bone marrow tests, a special needle is inserted into the hip or bone while your child is sedated, a small amount (about 1 teaspoon) of liquid bone marrow (looks like blood) is removed, and then a small piece of the bone marrow (the soft bony portion) is obtained. The bone marrow is viewed under a microscope to determine if any retinoblastoma cells are present. The results usually are available within 2–3 days of the procedures. The most common potential side effect is pain at the procedure site that lasts less than 24 hours. It is rare for a patient with retinoblastoma to have evidence of bone marrow disease unless the disease is very advanced. Not all children with retinoblastoma will need to have a bone marrow test.

LUMBAR PUNCTURE (SPINAL TAP)
This test is performed while your child is sedated and usually is done along with the bone marrow tests. While your child is lying on his or her side, a long, thin needle will be inserted a short distance (1–2 inches) into the lower middle portion of his or her back between two vertebrae (bones of the spine). This procedure is done to obtain a small amount of spinal fluid, a clear liquid that is then sent to the pathology lab and examined under a microscope to look for tumor cells. As with the bone marrow, it is rare for a patient with retinoblastoma to have spinal fluid that shows evidence of a tumor, unless the cancer is very advanced. Not all children with retinoblastoma will need to have a spinal tap test.

BONE SCAN
A bone scan is done to determine whether retinoblastoma has spread to any of the bones. A small amount of isotope (radioactive dye that makes any areas of tumor in the bone light up on the pictures) is injected into a vein. About 2–3 hours later, scans (pictures) are taken of your child’s entire body. The scanning process is painless; however, young children may need sedation to help them lie still during this scan. It is rare for a patient with retinoblastoma to have tumor metastasize to the bones. Not all children with retinoblastoma will need to have a bone scan.

BLOOD TESTS
Blood tests are done to monitor your child's blood cells, body salts, and chemistries. A complete blood count (CBC) is used to look for anemia, which is low hemoglobin (iron-containing blood product). A child who is anemic may appear pale and be more tired than usual. The CBC also will detect changes in
your child's white blood cells, which fight infection, and platelets, which are cells that help blood to clot properly. Tests of body salts and chemistries show how well your child's kidneys and liver are working. Many of these blood tests will be used to monitor your child throughout treatment. Some blood tests can be obtained from a finger prick; others must come from a vein or a venous access device (VAD), such as a Hickman line or a Port-a-Cath.

**VENOUS ACCESS DEVICE (VAD)**

A venous access device (VAD), sometimes called a central line, is a permanent intravenous (IV) tube that can be used for the duration of your child's therapy, including blood tests, medications, chemotherapy, blood products, antibiotics, and nutritional support when needed. In most cases, this device will prevent your child from undergoing a needle stick for any of the previously mentioned tests. A VAD is inserted when your child is under heavy sedation or anesthesia. The three types of VADs include a Hickman line (single or double lumen), an implanted port (small port placed under the skin), and a PICC line (a central line inserted through a vein in the arm). The decision to place a VAD and determine which type is best for your child during treatment will be made by you and your child's provider.

### HOW CAN RETINOBLASTOMA BE TREATED?

As with most childhood cancers, a combination of treatments are used to maximize the killing of cancer cells. For retinoblastoma, four types of therapy are commonly used: local, or focal, treatments directly to the eye(s); chemotherapy; surgery; and radiation. Each of these therapies will be described in more detail later in this section.

The type of therapy offered to your child will depend upon three main factors:
1. whether one or both eyes are affected
2. the stage of retinoblastoma in each eye
3. the presence and extent of disease elsewhere in the body.

Most of the children with unilateral retinoblastoma normally have advanced or high-stage disease with little or no potential for useful vision. In many cases, the recommended initial treatment is enucleation (removal of the eye). If the disease is only in the eye, no further treatment is needed. If the tumor extends into the optic nerve, chemotherapy also may be used. Children with bilateral disease need to have their treatment managed differently. Within the past 10 years, chemotherapy, rather than enucleation or radiation therapy, has become the initial mode of treatment for bilateral and multifocal retinoblastoma in combination with focal treatments.

Your child’s provider will speak with you about the best treatment for your child. One option might be to enroll your child in a current clinical trial (depending on the type and stage of retinoblastoma) if one is available. Ultimately, treatment decisions will be made collaboratively by you (the child's parents) and your child's provider.
FOCAL TREATMENTS

Focal treatment is the term used to describe direct treatments to the eye(s) that try to kill or shrink the size of the tumor. There are five types of focal treatments: cryotherapy (freezing), laser photocoagulation (clotting using laser light), thermotherapy (laser-created heat), radioactive plaque (radiation applied directly to the eye), and subconjunctival chemotherapy (direct injection of chemotherapy into the eye). These focal treatments usually are performed during the exam under anesthesia (EUA) when the child is asleep. After the procedure, your child may complain of some mild pain or have local swelling or redness of the treated eye.

CHEMOTHERAPY

Chemotherapy is treatment with medications that are known to kill tumor cells throughout the body. Although several chemotherapy medications are known to be effective in the treatment of retinoblastoma, chemotherapy alone cannot control this disease. Each of the medications kills the cancer cells in a different way, which is why certain chemotherapy medications are used together and on a particular schedule. For retinoblastoma, all chemotherapy drugs, other than subconjunctival treatments, are given through a vein or VAD. Your child’s doctor will discuss with you the specific chemotherapy treatments recommended for your child and any potential side effects.

Chemotherapy usually is given to children with multifocal unilateral (multiple tumors in one eye) and bilateral retinoblastoma because it helps shrink the tumors and aids focal eye treatments. It also is beneficial for children with advanced disease within the eye(s) or metastases, and those who are at higher risk of having the retinoblastoma spread.

RADIATION

Radiation therapy also is used in the treatment of retinoblastoma, usually in combination with other therapies or after other therapies have failed. There are two types of radiation therapy used for retinoblastoma: brachytherapy and external beam radiation therapy. Brachytherapy is a plaque (special radioactive patch) that is placed directly around the affected area of the eye. It is sewn to the skin that covers the eye while the child is under general anesthesia in the operating room. Side effects may include pain, swelling, and redness of the treated eye. The plaque remains in place for 3–5 days, depending on the dose of radiation that needs to be delivered, and then is removed while the child is under general anesthesia in the operating room. This form of treatment delivers concentrated radiation therapy only to the tumor without affecting the rest of the eye or the eye socket (bone). The child remains in the hospital during this process.

External beam radiation therapy is rarely given to a child younger than 1 year of age, but it may be used in older children. It consists of a very precise measured amount of radiation that is delivered to the affected orbit(s) every day over a period of 4–6 weeks. The length of time varies depending on the dose
of radiation needed. The radiation dose is calculated by a radiation oncologist (cancer doctor) who will explain exactly how and where the radiation will be given and any potential short- and long-term side effects that may occur. External beam radiation therapy can injure the entire eye and portions of the orbit (the bone around the eye). Because children with retinoblastoma who require external beam radiation therapy are usually 1–5 years of age and are still growing, the radiation can stunt the growth of the orbit.

**SURGERY**

Surgery is indicated for the treatment of retinoblastoma if the tumor is large enough to interfere with useful vision of the affected eye, or if all other forms of treatment (chemotherapy, radiation, and focal treatments) have been unsuccessful in killing the cancer. If surgery is necessary, the entire globe (the eyeball, which resembles a marble) is removed by the ophthalmologist in the operating room. This operation is called enucleation and is performed as a day surgery procedure. During the procedure, the ophthalmologist places a temporary implant called a conformer inside the orbit once the globe has been removed. The implant looks like part of a small golf ball and permanently takes the place of the globe because it maintains the shape of the eye. Your child will be unaware that the conformer is in place; it cannot be removed, other than by surgery, and is not visible. After the surgery, your child’s eyelids may be bruised and swollen for several days, but these local side effects will go away. Within 6–8 weeks after surgery, your child will be fitted with a prosthetic eye, which resembles a large contact lens. A special artist called an ocularist will make your child’s prosthetic eye by fitting the prosthetic eye and painting it to match your child’s remaining eye.

It will be placed inside of the eye socket between the eyelids and, if fitted properly, should not come out easily. The prosthetic eye will look almost as natural as the remaining eye, except it will not move as much from side to side or up and down.

**HOW LONG WILL MY CHILD’S THERAPY LAST?**

The length of your child’s therapy depends on the type and stage of your child’s tumor at the time of diagnosis. Usually, the treatment is given for several months. Follow-up blood tests and check-ups between and following treatments generally are done in the clinic or doctor’s office. Your child will require annual or semianual checkups throughout his or her entire life.

**WHAT NEW METHODS OF TREATMENT ARE THERE?**

Most of the advances in the treatment of childhood cancer have been made through a process known as clinical trials. In many clinical trials, the best known (standard therapy) treatment for a particular cancer is compared with a new (experimental therapy) treatment that is believed to be at least as good as, and possibly better than, the standard treatment. Clinical trials allow providers to determine whether promising new treatments are safe and effective. Participation in clinical trials is voluntary. Because clinical trials involve research with new treatment plans, all of the risks cannot be known ahead of time, and unknown side effects may occur. However, children who participate in clinical trials can be among the first to benefit
from new treatment approaches. Before making a decision about your child's participation in a clinical trial, you should discuss the risks and potential benefits with your child's provider and treatment team.

More information about clinical trials is available in the free booklet Taking Part in Clinical Trials: What Cancer Patients Need to Know (National Cancer Institute Publication No. 98-4250). To obtain the booklet along with other useful information about childhood cancer, call 800/4CANCER (800/422-6237) or visit the National Cancer Institute website at www.cancer.gov/cancertopics/types/retinoblastoma.

WHAT ARE MY CHILD’S CHANCES OF GETTING ANOTHER CANCER?

Children who have the genetic form of retinoblastoma are at a greater risk of getting another form of cancer than children who do not have the genetic form. It is believed that after the original diagnosis, the chance of another cancer occurring increases by about 1% a year. The most common types of second cancers are tumors of the bone, muscle, and skin. It is important that retinoblastoma patients continue to receive annual physical exams throughout their lives. If a second cancer occurs, the chance of cure increases the earlier it is found and treated.

HOW CAN I WORK WITH THE HEALTHCARE TEAM?

Your child’s care requires a team approach. As a parent, you are a major part of the team, and your input is very important. Because you know your child better than anyone else, the medical and nursing staff will need your help as they provide comprehensive management for the disease.

It is important to communicate openly with your child’s healthcare team. Be sure to question your child’s providers about anything of which you are not sure. It helps to write down your questions as you think of them.

Here are some examples of questions to ask:
• Which kind of cancer does my child have?
• Has the cancer spread beyond the primary (original) site?
• What is the stage of the cancer, and what does that mean?
• What treatment choices are available?
• Which treatment(s) do you recommend and why?
• What are the risks or side effects during and after the recommended treatment?
• What can we do to prepare for treatment?
• What is my child’s outlook for survival?
• What are the chances of a recurrence?
Use this space to write down some additional questions:
ARE MY FEELINGS NORMAL AND WHAT CAN I DO ABOUT THEM?

Hearing that your child has cancer is shocking and overwhelming. At first, you may not believe it, or you may hope that the diagnosis is wrong. However, the changes you see in your child and the experience of being in the hospital and beginning treatment will confirm the reality of your child's situation.

Many family members feel that they are somehow responsible for their child's disease, or they feel guilty that they were not able to detect it sooner. Remember that this disease often does not become noticeable until it is quite advanced, so there may have been no way of detecting it in the early stages. Besides feeling shock and guilt, you and your family will probably feel anger and sadness. Even the youngest family members are likely to be affected. These feelings are normal, and each family member will express these emotions in different ways and at different times. It can be very difficult to feel so many strong emotions all at once. Talking honestly with each other about feelings, reactions, and questions will help everyone in the family. It may seem difficult to talk to friends, family, or even medical staff, but expressing your feelings will help you cope. Your child will benefit if his or her loved ones continue to show their caring through support and communication.

HOW CAN I HELP MY CHILD?

As a parent, you will often notice various changes in your child during treatment. These changes or symptoms can make you feel even more helpless. The changes are due to both the disease and the treatment. It is important to remember that although there may be changes on the outside, your child is still the same person on the inside. Some changes in body appearance, such as hair loss, can be temporary; others, such as having different sized and shaped eye sockets, can be permanent. These changes often bother adults much more than a young child or a child’s siblings or friends. All of your feelings about what your child is going through during treatment must be balanced by remembering that treatment provides an opportunity to cure the disease, preserve as much vision as possible, and have your child go on to live a full, meaningful, and productive life.

It is important to reinforce to your child that nothing he or she did or said caused the retinoblastoma. Likewise, telling your child that your anger or sad feelings are directed at the tumor and not at him or her will help keep your special relationship honest and close. Like you, your child will need to share feelings with someone he or she can trust. Do not be afraid to ask your child to express his or her feelings, and do not be afraid to explain what is happening and why.

In spite of your child’s disease, he or she is still growing and learning. All children, sick and well, need love, attention, discipline, limits, and the opportunity to try new skills and activities.

As you begin to learn the new, special needs of your child, it is important to remember that he or she still has all the needs and rights of any growing, developing person. Do not avoid using direct terms and explanations with your child. Children will tolerate treatment better if they understand it and are allowed to be active decision-makers whenever possible—the same is true for parents!
IS MY CHILD’S DIET IMPORTANT DURING THE TREATMENT?

Yes. We know from research that well-nourished children tolerate therapy better and have fewer treatment delays from illness. It may be difficult for your child to resume normal eating habits while on therapy, so you will need to be flexible and creative. Often, numerous small meals will be tolerated better than three large ones. Offer foods high in protein and carbohydrates. A dietitian trained in the calorie and energy needs of children can offer you guidance. Multivitamins and all medicines not specifically prescribed for your child by the team treating the retinoblastoma should be approved by your doctor before you give them to your child because there may be some interactions between them and the chemotherapy your child is receiving.

Children will be more interested in eating foods that they help prepare. It is important to include your child in the social activity of family meals even if full meals are not eaten. Nobody wins food fights—it is best not to force your child to eat. The medical staff can intervene if a nutritional problem develops.

CAN MY CHILD ATTEND SCHOOL DURING TREATMENT?

Because most children with retinoblastoma are infants and toddlers, they are not yet attending school. Your child may have visual problems ranging from limited sight to complete blindness that can affect his or her adjustment to normal activities and school work when he or she is old enough to attend. Your child, regardless of age, should have his or her vision checked to determine vision level and be referred for services for children with vision limitations. Many of these services are available through the public school system, beginning with “infant stimulation” programs for infants and toddlers. These services are usually accessed by calling your local school district. The earlier your child begins receiving visual and infant stimulation services, the better he or she will adjust to any vision impairments. Children older than 3 years of age who develop sight problems are able to receive special services through the local school district.

Your child’s ability to attend day care, preschool, or school during treatment will depend on the intensity of the therapy and his or her response to treatment. Some children tolerate therapy better than others. Your child may not be able to attend school for extended periods because of the treatment, side effects, or hospitalization. However, it is important that your child keep up with school work. Talk to someone (teacher, principal, or counselor) at your child’s school about arranging educational services until he or she is able to return to school. You also should discuss school attendance with your child’s doctor or nurse. Many pediatric hospitals have programs that enable children to attend school while hospitalized. Your child’s school also may be able to arrange for a home tutor to provide instruction for your child.

School is important in helping children maintain social contact with their peers. Therefore, it is important for your child to return to school as soon as he or she is physically and medically able to do so. Maintaining time with friends will be an important part of your child’s recovery and will ease the adjustment when he or she returns to school.
WHERE CAN I GO FOR MORE INFORMATION ABOUT RETINOBLASTOMA?

The following websites have a wealth of information about retinoblastoma:

www.cancerindex.org
www.curesearch.org
www.instituteforfamilies.org
www.retinoblastoma.net
www.stjude.org

You also can consult the following supplemental educational booklet: My Fake Eye (English or Spanish) by Nancy Mansfield, Institute for Families of Blind Children, 1300 N. Vermont Ave., Los Angeles, CA 90027, 323/669-4649.

REFERENCES


