Ewing Family of Tumors

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide to make new cells, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. In most cases the cancer cells form a tumor. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but often the DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. In adults, sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named (and treated) based on the place where it started. For example, breast cancer that has spread to the liver is still breast cancer,

not liver cancer. Likewise, prostate cancer that has spread to the bone is still prostate cancer, not bone cancer.

Different types of cancer can behave very differently. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called *benign*. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

What are the differences between cancers in adults and children?

The types of cancers that develop in children are often different from those that develop in adults. Childhood cancers are often the result of DNA changes in cells that take place very early in life, sometimes even before birth. Unlike many cancers in adults, childhood cancers are not strongly linked to lifestyle or environmental risk factors.

There are exceptions, but childhood cancers tend to respond better to treatments such as chemotherapy. Children's bodies also tend to tolerate chemotherapy better than adults' bodies do. But cancer treatments such as chemotherapy and radiation therapy can have some long-term side effects, so children will need careful attention for the rest of their lives.

Since the 1960s, most children and teens with cancer have been treated at specialized centers designed for them. Being treated in these centers offers the advantage of a team of specialists who know the differences between adult and childhood cancers, as well as the unique needs of children with cancers. This team usually includes pediatric oncologists, surgeons, radiation oncologists, pathologists, pediatric oncology nurses, and nurse practitioners.

These centers also have psychologists, social workers, child life specialists, nutritionists, rehabilitation and physical therapists, and educators who can support and educate the entire family.

Most children with cancer in the United States are treated at a center that is a member of the Children's Oncology Group (COG). All of these centers are associated with a university or children's hospital. As we have learned more about treating childhood cancer, it has become even more important that treatment be given by experts in this area.

Any time a child or teen is diagnosed with cancer, it affects every family member and nearly every aspect of the family's life. You can read more about coping with all these changes in our document, *Children Diagnosed With Cancer: Dealing With Diagnosis.*

What is the Ewing family of tumors?

The Ewing family of tumors is a group of cancers that start in the bones or nearby soft tissues that share some common features. They can develop at any age, but these tumors are most common in early teenage years. There are 3 main types of Ewing tumors:

- **Ewing sarcoma of bone:** Ewing sarcoma that starts in the bone is the most common tumor in this family. This type of tumor was first described by Dr. James Ewing in 1921, who found it was different from the more common bone tumor, osteosarcoma. Its cells looked different from osteosarcoma cells when seen under a microscope. It was also more likely to respond to radiation therapy.

- **Extraosseous Ewing tumor (EOE):** Extraosseous Ewing tumors start in soft tissues around bones, but they look and act very much like Ewing sarcomas in bones. They are also known as *extraskeletal* Ewing sarcomas.

- **Peripheral primitive neuroectodermal tumor (PPNET):** This rare childhood cancer also starts in the bone or soft tissue and shares many features with Ewing sarcoma of bone and EOE. Peripheral PNETs that start in the chest wall are known as *Askin tumors*. (Peripheral PNETs are similar to, but not quite the same as, PNETs of the brain and spinal cord. For more information on those tumors, see our document, *Brain and Spinal Cord Tumors in Children*.)

Researchers have found that the cells that make up Ewing sarcoma, EOE, and PPNET are very similar. They tend to have the same DNA (gene) abnormalities and share similar proteins, which are rarely found in other types of cancers. That's why these 3 cancers are thought to develop from the same type of cells in the body. There are slight differences among these tumors, but they all get the same treatment.

Most Ewing tumors occur in the bones. The most common sites are the pelvis (hip bones), the chest wall (such as the ribs or shoulder blades), and the legs, mainly in the middle of the long bones. (In contrast, osteosarcoma usually occurs at the ends of the long bones, especially around the knees.) Extraosseous Ewing tumors can occur almost anywhere.

Most Ewing tumors occur in children and teens, but they can also occur in adults. **This document focuses on Ewing tumors in children and teens, but most of the information here (including much of the treatment information) applies to Ewing tumors in adults as well.**

What are the key statistics about Ewing tumors?

Only about 1% of all childhood tumors are Ewing tumors. About 225 children and teens are diagnosed with Ewing tumors in North America each year.

Most Ewing tumors occur in teens, but they can also affect adults (mainly in their 20s and 30s), as well as younger children.

Slightly more males than females develop these cancers. Most of the patients are white, either non-Hispanic or Hispanic. This disease is very rare among African Americans, and it also seldom occurs in other racial groups.

Survival statistics for these tumors are discussed in the section “Survival rates for Ewing tumors, by stage.”

What are the risk factors for Ewing tumors?

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 Ewing tumors.

Studies of children with Ewing tumors have not found links to radiation, chemicals, or any other environmental exposures.

Certain childhood cancers tend to run in some families. But genetic changes passed along within families are not an important risk factor for Ewing tumors. Although the gene changes that cause most Ewing tumors are known (see the section “Do we know what causes Ewing tumors?”), they are not inherited.

Race/ethnicity

Ewing tumors occur most often in whites (either non-Hispanic or Hispanic). They are less common among Asian Americans and are extremely rare among African Americans. The reason for this is not known.

Gender

These cancers are slightly more common in males than in females.

Age

Ewing tumors can occur at any age, but they are most common in teens and are less common among young adults and young children. They are rare in older adults.

Do we know what causes Ewing tumors?

The cause of Ewing tumors is not fully understood, but researchers are learning how certain changes in a cell's DNA can cause the cell to become cancerous. DNA is the chemical in each of our cells that makes up our genes. Genes tell our cells how to function. They are packaged in chromosomes, which are long strands of DNA in each cell. We normally have 23 pairs of chromosomes in each cell (one set of chromosomes comes from each parent). We usually look like our parents because they are the source of our DNA. But DNA affects more than how we look.

Some genes control when our cells grow, divide into new cells, and die. Certain genes that help cells grow and divide are called *oncogene*s. Others that slow down cell division or make cells die at the right time are called *tumor suppressor genes*. Cancers can be caused by DNA mutations (or other types of changes) that turn on oncogenes or turn off tumor suppressor genes.

Researchers have found chromosome changes that lead to Ewing tumors, but these changes are not inherited. Instead, they develop in children after birth, in a single cell, for no known reason.

Nearly all Ewing tumor cells have changes that involve the *EWS* gene, which is found on chromosome 22. In most cases, the change is a swapping of pieces of DNA (called a *translocation*) between chromosomes 22 and 11. Less often, the swap is between chromosomes 22 and 21, or rarely between 22 and another chromosome. The translocation moves a certain piece of chromosome 11 (or another chromosome) just next to the *EWS* gene on chromosome 22, causing the *EWS* gene to be turned on all the time. Activation of the *EWS* gene leads to overgrowth of the cells and to the development of this cancer, but the exact way in which this happens is not yet clear.

Lab tests can be used to find chromosomal translocations in Ewing tumor cells (see the section, "How are Ewing tumors diagnosed?"). If doctors are not sure if a tumor belongs to the Ewing family, they can use these tests to confirm the diagnosis.

The gene changes that lead to Ewing tumors are now fairly well known, but it's still not clear what might cause these changes. It may just be a random event that sometimes happens inside a cell, without having an outside cause. There are no known lifestyle-related or environmental causes of Ewing tumors, so it is important to remember that there is nothing these children or their parents could have done to prevent these cancers.

Can Ewing tumors be prevented?

The risk of many adult cancers can be reduced with certain lifestyle changes (such as staying at a healthy weight or quitting smoking), but at this time there are no known ways to prevent most cancers in children.

The only known risk factors for Ewing tumors (age, gender, and race/ethnicity) cannot be changed. There are no known lifestyle-related or environmental causes of Ewing tumors, so at this time there is no way to protect against these cancers.

Can Ewing tumors be found early?

Ewing tumors are uncommon, and there are no widely recommended screening tests for these tumors. (Screening is testing for cancer in people without any symptoms.) Still, Ewing tumors are sometimes found early, before they have spread widely.

The most common symptom of a Ewing tumor is pain in the area of the tumor. In some cases the tumor may show up as a lump or swelling on an arm, leg, or the trunk. Sometimes the lump feels warmer than the rest of the body, and in some cases the child may have general symptoms like a fever or not feeling well.

Of course, children and teens often get sore or have lumps and bumps from normal activities. But pains or lumps that don’t go away should be checked by a doctor. The same is true if a lump feels warm and/or the child has a fever. These symptoms are more likely to have other causes, such as an infection, but they need to be checked by a doctor so that the cause can be found and treated, if needed.

How are Ewing tumors diagnosed?

Ewing tumors are usually found as a result of signs or symptoms that a child or teen is having. If a tumor is suspected, tests will be needed to confirm the diagnosis.

Signs and symptoms of Ewing tumors

Pain

The most common symptom of a Ewing tumor is pain at the tumor site. Most patients with bone tumors have bone pain. The pain may be caused by the tumor spreading under the outer covering of the bone (periosteum), or the pain may be from a break or a fracture of a bone that has been weakened by the tumor.

Lump or swelling

Over time, most Ewing bone tumors and almost all non-bone (soft tissue) Ewing tumors cause a swelling or mass, which is more likely to be noticed in tumors in the arms or legs. The tumor may feel soft and warm. Tumors in the chest wall and pelvic tumors may not be noticed until they have grown quite large.

Other symptoms

If the tumor has spread, the child may have a fever, feel very tired, or even lose weight. Rarely, tumors near the spine can cause weakness, numbness, or paralysis in the arms or legs, while tumors that have spread to the lungs can cause shortness of breath.

Many of the signs and symptoms of Ewing tumors are more likely to be caused by something else. Still, if your child has any of these symptoms, see a doctor so that the cause can be found and treated, if needed.

Because many of these signs and symptoms can be confused with normal bumps and bruises or bone infections, Ewing tumors may not be recognized right away. The correct diagnosis is often made only after the child's bone is x-rayed when the condition does not go away (even with antibiotics) or gets worse.

Medical history and physical exam

If your child has signs or symptoms that might suggest a tumor, the doctor will want to get a complete medical history to learn about any symptoms the child is having and how long they have been present. The doctor will also do a complete physical exam, paying special attention to any areas causing pain or swelling.

If symptoms and/or the results of the physical exam suggest a child might have a Ewing tumor (or other tumor), the doctor will do tests to find out. These might include imaging tests, biopsies, and/or lab tests.

Imaging tests

Imaging tests (such as x-rays, MRI scans, CT scans, bone scans, and PET scans) create pictures of the inside of the body. Imaging tests may be done for many reasons, including:

- To help find out if a suspicious area might be cancerous
- To determine the extent of a tumor or learn how far a cancer may have spread
- To help determine if treatment has been effective

Patients who have or may have a Ewing tumor will have one or more of these tests.

X-rays

If a bone lump doesn't go away or the doctor suspects a bone tumor for some other reason, an x-ray of the area will probably be the first test done. A radiologist (doctor who specializes in reading imaging tests) can usually spot a bone tumor on an x-ray and can often tell if it is

likely to be a Ewing tumor that involves bone. But other imaging tests may be needed as well.

Even if an x-ray strongly suggests a Ewing bone tumor, a biopsy (described below) is always needed to confirm that it is cancer rather than some other problem, such as an infection.

Magnetic resonance imaging (MRI) scan

Often, an MRI scan is done to better define an abnormal area seen on an x-ray. MRI scans can usually tell if it is likely to be a tumor, an infection, or some type of bone damage from other causes. MRI scans can also help determine the exact extent of a tumor, as they provide a detailed view of the marrow inside bones and the muscle, fat, and connective tissue around the tumor. Defining the extent of the tumor is very important when planning surgery or radiation therapy.

MRI scans might also be done to see if the cancer has possibly spread to other areas, such as the spine or pelvis (hip area). MRI scans can also be used during and after treatment to see how well the tumor is responding.

MRI scans create detailed images of soft tissues in the body. They do this using radio waves and strong magnets instead of x-rays, so there is no radiation involved. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image. A contrast material called *gadolinium* may be injected into a vein before the scan to better see details.

MRI scans may take up to an hour. Your child may have to lie inside a narrow tube, which is confining and can be distressing. 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. Sometimes, younger children are given medicine to help keep them calm or even asleep during the test.

Computed tomography (CT or CAT) scan

CT scans of the chest are often used to see if a Ewing tumor has spread to the lungs. MRI scans are usually a bit better at defining the extent of the main tumor itself, but a CT scan of the tumor may be done as well.

The CT scan is an x-ray test that produces detailed cross-sectional images of parts of the body, including soft tissues such as muscles. 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 be asked to drink a contrast solution and/or get an intravenous (IV) injection of a contrast dye that helps better outline abnormal areas in the

body. If a contrast dye is to be injected, your child may need an IV line. The contrast may 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 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 in the middle opening. Your child will need to lie still on the table while the scan is being done. During the test, the table slides in and out of the scanner. Some people feel a bit confined while the pictures are being taken. In some cases, your child may need to be sedated before the test to stay still and help make sure the pictures come out well.

Bone scan

A bone scan can help show if a cancer has metastasized (spread) to bones in other parts of the body, and might be part of the workup for a child with a Ewing tumor. This test is useful because it can show the entire skeleton at once. (A positron emission tomography [PET] scan can often provide similar information, so in some cases a bone scan may not be needed if a PET scan is done.)

For a bone scan, 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 substance settles in areas of damaged bone throughout the entire skeleton 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.

Areas of active bone changes appear as “hot spots” on the skeleton because they attract the radioactivity. These areas may suggest the presence of cancer, but other bone diseases can also cause the same pattern. To be sure, other tests such as plain x-rays or MRI scans, or even a bone biopsy might be needed.

Positron emission tomography (PET) scan

For a PET scan, a form of radioactive sugar (known as *fluorodeoxyglucose* or *FDG*) is injected into the blood. The amount of radioactivity used is very low and will pass out of the body within a day or so. Because cancer cells in the body are growing quickly, they absorb large amounts of the sugar. After waiting about an hour, your child will lie on a table in the PET scanner for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it provides helpful information about the whole body.

PET scans can be very helpful in showing the spread of Ewing tumors and in finding out whether abnormal areas seen on other imaging tests (such as a bone scan or CT scan) are tumors. PET scans can also be repeated during treatment to monitor the cancer over time.

Some newer machines can do a PET and CT scan at the same time (PET/CT scan). This lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT scan.

Biopsy of the tumor

The results of imaging tests may strongly suggest a Ewing tumor, but a biopsy (removing some of the tumor for viewing under a microscope and other lab testing) is the only way to be certain. A biopsy is also the best way to tell Ewing tumors from other types of cancer.

If the tumor involves bone, it is very important that a doctor experienced in treating Ewing tumors perform the biopsy. Whenever possible, the biopsy and the surgery to treat the cancer should be planned together, and the same orthopedic surgeon should do both. Proper planning of the biopsy location and technique can help prevent later complications and reduce the amount of surgery needed later on during treatment.

There are a couple of ways to get a sample of the tumor to diagnose Ewing tumors.

Excisional biopsy

In very rare cases, if the tumor is small enough and in a good location, the surgeon can completely remove it while the child is under general anesthesia (asleep). This is called an *excisional biopsy*.

Incisional biopsy

In most cases of suspected Ewing tumors, an incisional biopsy (taking only a piece of the tumor) is more likely to be done. The surgeon can do this either during an operation by cutting away a piece of the tumor through an opening on the skin (known as an *open biopsy*) or by placing a large, hollow needle through the skin and into the tumor (known as a *needle biopsy* or *closed biopsy*).

Incisional biopsies in older teens and adults are sometimes done using a local anesthetic (numbing medicine), but in children they are more often done while the child is under general anesthesia (asleep).

If a child is going to have general anesthesia for the biopsy, the surgeon may also plan other procedures while the child is asleep to avoid having to do them as separate operations later on. For example, if the tumor is thought to have spread to the chest or elsewhere, the surgeon may take a biopsy of these suspected tumors when the child is still asleep. The doctor may

also do a bone marrow biopsy (see next section) at this time to see if the cancer has spread to the bone marrow spaces.

During the biopsy (while the child is still asleep), a pathologist (a doctor specializing in using lab tests to diagnose diseases) can take a quick look at the biopsy sample under the microscope. If it looks like a Ewing tumor, the child will very likely need chemotherapy as part of treatment, so the surgeon may place a small flexible tube, known as a *central venous catheter*, into a main blood vessel in the chest area during the same operation. The catheter end lies just under or outside on the skin, which gives doctors and nurses easier access to the large vein. The catheter will stay in place for several months during treatment. This allows the child to get fewer needle sticks when chemotherapy is given at a later time. (See the "Chemotherapy" section.)

Bone marrow aspiration and biopsy

These tests are used to see if the cancer cells have spread into the bone marrow, the soft inner parts of certain bones. The tests aren't usually done to diagnose Ewing tumors, but they may be done once the diagnosis is made because it is important to know if the tumor has spread to the bone marrow.

Bone marrow aspiration and biopsy are usually done at the same time. In most cases the marrow samples are taken from the back of both of the pelvic (hip) bones.

These tests may be done as a separate procedure, or they may be done during the surgery to biopsy or treat the main tumor (while the child is still under anesthesia).

If the bone marrow *aspiration* is being done as a separate procedure, the child lies on a table (on his or her side or belly). After the area over the hip is cleaned, the skin and the surface of the bone are numbed with a local anesthetic, which may cause a brief stinging or burning sensation. In most cases, the child is also given other medicines to make them sleepy, or they might even be asleep during the procedure. A thin, hollow needle is then inserted into the bone, and a syringe is used to suck out 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 twisted as it is pushed down into the bone. Once the biopsy is done, pressure is applied to the site to help stop any bleeding.

Samples from the bone marrow are sent to a pathology lab, where they are looked at and tested for cancer cells.

Testing the biopsy samples

A doctor called a pathologist looks at all biopsy specimens under a microscope to see if they contain cancer cells. If cancer is found, the specific type of cancer can often be determined as

well. But because cells from Ewing tumors share many of the same features as cells from other types of childhood cancer, more lab tests are often needed.

Immunohistochemistry

For this test, a portion of the biopsy sample is treated with special proteins (antibodies) that attach to substances found on Ewing tumor cells but not on other cancers. Chemicals (stains) are then added so that cells containing these substances change color and can be seen under a microscope. This lets the pathologist know that the tumor is in the Ewing family.

Cytogenetics

For this test, chromosomes (pieces of DNA) from the tumor cells are looked at under a microscope to detect any changes. Ewing tumor cells usually have chromosome translocations, where 2 chromosomes swap pieces of their DNA. In most cases, the cells have translocations between chromosomes 22 and 11. Less often, the translocation is between other chromosomes. Finding these changes can help doctors tell Ewing tumors from other types of cancer. Other types of chromosome changes may also be found in some Ewing tumors.

Getting the results of cytogenetic testing usually takes about 2 to 3 weeks because the cancer cells must be grown in lab dishes for a couple of weeks before their chromosomes can be seen under the microscope.

Fluorescence in situ hybridization (FISH) is a type of cytogenetic test that uses special fluorescent dyes to spot specific chromosome changes in Ewing tumors. FISH can find most chromosome changes (such as translocations) that are visible under a microscope in standard cytogenetic tests, as well as some changes too small to be seen with usual cytogenetic testing.

FISH can be used to look for specific changes in chromosomes. It can be used on blood or bone marrow samples. It is very accurate and can usually provide results within a couple of days.

Reverse transcription polymerase chain reaction (RT-PCR)

This test is another way to find translocations in tumor cells to confirm the type of tumor. RT-PCR is a very sensitive test that is often able to detect very small numbers of cells with translocations, which wouldn’t be detected by cytogenetics.

RT-PCR is also useful in looking for left over or recurrent cancer after treatment. For example, if RT-PCR testing of a bone marrow sample after treatment finds cells with a typical translocation, it is likely that the cancer has not been cured, so more treatment is likely to be needed.

Blood tests

No blood test can be used to diagnose Ewing tumors. But certain blood tests may be helpful once a diagnosis has been made.

A complete blood count (CBC) measures the levels of white blood cells, red blood cells, and platelets in the blood. An abnormal CBC result at the time of diagnosis might suggest the cancer has spread to the bone marrow, where these blood cells are made.

A blood test for levels of an enzyme called *lactate dehydrogenase* (LDH) is typically done at diagnosis. A high LDH level indicates the cancer may be harder to treat.

Standard blood tests are done often to check a child's general health both before treatment (especially before surgery) and during treatment (such as chemotherapy) to look for possible problems or side effects. These tests often include complete blood counts to monitor bone marrow function and blood chemistry tests to measure how well the liver and kidneys are working.

How are Ewing tumors staged?

Once a Ewing tumor has been diagnosed, tests are done to determine the stage (extent of spread) of the cancer. The stage of a Ewing tumor is one of the most important factors determining a person's outlook (prognosis) and in choosing treatment.

The stage is based on results of imaging tests and biopsies of the main tumor and other tissues, which were described in the section "How are Ewing tumors diagnosed?"

A staging system is a standard way in which the cancer care team describes the extent of the cancer. The formal (and more detailed) staging system for Ewing tumors is the American Joint Committee on Cancer (AJCC) system for bone cancer. It is described here to help you understand it, in case your doctor refers to it. But for practical purposes, doctors often use a simpler system, dividing Ewing tumors into localized or metastatic groups. This is described below as well.

AJCC staging system for bone cancer

The AJCC has developed staging systems for most types of cancers. The AJCC uses one system to describe all bone cancers, including Ewing tumors that start in bone. Extraosseous Ewing (EOE) tumors (Ewing tumors that don't start in bones) are staged differently. They are staged like soft-tissue sarcomas. Information about soft-tissue sarcoma staging can be found in our document, *Sarcoma - Adult Soft Tissue Cancer*.

The AJCC staging system for bone cancers is based on 4 key pieces of information:

- **T** describes the size of the main (primary) **tumor** and whether it appears in different areas of the bone.
- **N** describes the extent of spread to nearby (regional) lymph **nodes** (small bean-shaped collections of immune system cells). Bone tumors rarely spread to the lymph nodes.
- **M** indicates whether the cancer has **metastasized** (spread) to other organs of the body. (The most common sites of spread are to the lungs or other bones.)
- **G** stands for the **grade** of the tumor, which describes how the cells from biopsy samples look under a microscope. Low-grade tumor cells look more like normal cells, and are less likely to grow and spread quickly, while high-grade tumor cells look more abnormal. (All Ewing tumors are considered high-grade tumors.)

Numbers or letters appear after T, N, M, and G to provide more details about each of these factors.

T categories of bone cancer

T0: There is no evidence of a main (primary) tumor

T1: The tumor is 8 cm (around 3 inches) across or less

T2: The tumor is larger than 8 cm across

T3: The tumor is in more than one site in the same bone

N categories of bone cancer

N0: There is no spread to regional (nearby) lymph nodes

N1: The cancer has spread to nearby lymph nodes

M categories of bone cancer

M0: There is no spread (metastasis) to distant organs

M1a: The cancer has spread only to the lungs

M1b: The cancer has spread to other distant sites in the body

Grades of bone cancer

GX: Grade cannot be assessed

G1-G2: Low grade

G3-G4: High grade

(All Ewing tumors are considered G4.)

TNM stage grouping

Once the T, N, and M categories and the grade of the bone cancer have been determined, the information is combined and expressed as an overall stage. The process of assigning a stage number is called *stage grouping*. The stages are described in Roman numerals from I to IV (1-4), and are sometimes divided further.

Stage IA*

T1, N0, M0, G1 to G2 or GX: The tumor is 8 cm across or less and is low grade (or the grade can't be assessed). The cancer has not spread to nearby lymph nodes or to distant parts of the body.

Stage IB*

T2 or T3, N0, M0, G1 to G2 or GX: The tumor is either larger than 8 cm across (T2) or it is in more than one place in the same bone (T3). It is low grade (or the grade can't be assessed). The cancer has not spread to nearby lymph nodes or to distant parts of the body.

Stage IIA

T1, N0, M0, G3 to G4: The tumor is 8 cm across or less and is high grade. The cancer has not spread to nearby lymph nodes or to distant parts of the body.

Stage IIB

T2, N0, M0, G3 to G4: The tumor is larger than 8 cm across and is high grade. The cancer has not spread to nearby lymph nodes or to distant parts of the body.

Stage III

T3, N0, M0, G3 to G4: The tumor is in more than one place in the same bone. It is high grade. The cancer has not spread to nearby lymph nodes or to distant parts of the body.

Stage IVA

Any T, N0, M1a, any G: The tumor has spread only to the lungs. It has not spread to the lymph nodes or to other distant sites. (It can be any size or grade.)

Stage IVB (if either of these applies)

Any T, N1, any M, any G: The tumor has spread to lymph nodes. It can be any size or grade, and may or may not have spread to other distant sites.

Any T, any N, M1b, any G: The tumor has spread to distant sites other than the lungs. It can be any size or grade.

*All Ewing tumors are classified as G4 (high grade), so they are never stage I bone cancers.

Localized vs. metastatic stages

In practice, doctors use a simpler system for staging Ewing tumors to determine how best to treat them. In this system, the cancers are classified as either localized or metastatic.

Localized Ewing tumors

A localized Ewing tumor is thought to be confined to the area where it started and may also have reached nearby tissues such as muscle or tendons. A Ewing tumor is considered localized only after all of the imaging tests (x-rays, CT or MRI scans, and PET or bone scans) and the bone marrow biopsy and aspirate do not find distant spread to other organs.

Even when imaging tests do not show that the cancer has spread to distant areas, many patients are likely to have *micrometastases* (very small areas of cancer spread that can't be detected with tests). This is why chemotherapy, which can reach all parts of the body, is an important part of treatment for all Ewing tumors.

Metastatic Ewing tumors

A metastatic Ewing tumor is one that has clearly spread from where it started to distant parts of the body. Most of the time, it spreads to the lungs or to other bones or the bone marrow. Less commonly, it spreads to the liver or lymph nodes.

About 1 in 4 patients will have obvious spread that is found by imaging tests. But as mentioned above, many other patients are likely to have small amounts of cancer spread to other parts of the body that can't be seen on imaging tests.

Survival rates for Ewing tumors by stage

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some people may want to know the survival statistics for those in similar situations, while others may not find the numbers helpful, or may even not want to know them. If you do not want to read about survival statistics for Ewing tumors, skip to the next section.

The 5-year survival rate refers to the percentage of patients who live *at least 5 years* after their cancer is diagnosed. Of course, many people live much longer than 5 years (and many are cured).

In order to get 5-year survival rates, doctors have to look at people who were treated at least 5 years ago. Improvements in treatment since then may result in a more favorable outlook for patients now being diagnosed with Ewing tumors.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any individual case. The stage of a person's cancer is important in estimating their outlook. But many other factors may also affect a person's outlook, such as their age, the location of the tumor, and how well the cancer responds to treatment.

Localized tumors

With current treatment, the overall 5-year survival rate for patients with Ewing tumors that are still localized when they are first found is around 70%.

Metastatic tumors

When the cancer has already spread at the time of diagnosis, the 5-year survival rate is about 15% to 30%. The survival rate is slightly better if the cancer has only spread to the lungs as opposed to having reached other organs.

Other factors affecting prognosis

Factors other than the stage of the cancer can also affect survival rates. Factors that have been linked with a better prognosis include:

- Smaller tumor size
- Main tumor is on an arm or leg (as opposed to chest wall or pelvis)
- Normal blood LDH level
- Good tumor response to chemotherapy
- Age younger than 10

Even when taking these other factors into account, survival rates are at best rough estimates. Your child's doctor is your best source of information on this topic, as he or she is familiar with your situation.

How are Ewing tumors 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.

Treatment overview for Ewing tumors

The main goals of treatment of Ewing tumors are:

- To try to cure the patient
- To keep as much function in affected parts of the body as possible
- To keep the long-term complications of treatment to a minimum

Achieving these goals requires a team approach that includes many types of doctors and other specialists. Surgeons, medical or pediatric oncologists, radiation oncologists, pathologists, psychosocial specialists, and rehabilitation specialists work together to give patients the best treatment and quality of life possible. For children and teens, this can be best done at a children's cancer center.

A child's cancer treatment often involves meeting a lot of different experts and learning more than you ever wanted to know about the health system. You can find out more in our document, Children Diagnosed With Cancer: Understanding the Health Care System.

Most patients with Ewing tumors are treated in clinical trials according to national treatment guidelines called *protocols*. In the United States, some of the most successful protocols have been those of the Children's Oncology Group and its forerunners. Studies from similar groups in Europe have also produced very important information. Most advances in the treatment of Ewing tumors have come from the results of these clinical trials.

The types of treatment that can be used in Ewing tumors include:

- Chemotherapy
- Surgery
- Radiation therapy
- High-dose chemotherapy followed by a stem cell transplant

Chemotherapy is almost always the first treatment. Localized therapy (surgery and/or radiation therapy) is next, often followed by more chemotherapy. A stem cell transplant might be an option for some patients with Ewing tumors that are unlikely to be cured with other treatments.

The next few sections describe the types of treatments used for Ewing tumors. This is followed by a description of the most common approaches to treatment based on the stage (extent) of the cancer.

Chemotherapy for Ewing tumors

Chemotherapy (chemo) is the use of anti-cancer drugs delivered through a vein or, rarely, by mouth in the form of pills. These drugs enter the bloodstream and affect cancer cells in all parts of the body, which makes this treatment useful for cancers that are likely to have spread.

Chemotherapy is an important part of treatment for just about all patients with Ewing tumors. It is typically the first treatment given, followed by surgery and/or radiation therapy. More chemotherapy is often given after the surgery and/or radiation is done.

As noted in the section “How are Ewing tumors staged?”, even patients with localized Ewing tumors, who have no obvious cancer spread in bone marrow samples or on imaging tests, are likely to have areas of cancer spread that are too small to be seen with these tests. If these patients do not get chemotherapy, these small metastases would eventually develop into larger tumors.

Doctors give chemo in cycles, with a period of treatment (often a few days in a row) followed by a rest period to give the body time to recover. A combination of several chemo drugs is used to treat patients with Ewing tumors. In the United States, the most common regimen alternates between 2 combinations of drugs given every 2 to 3 weeks (known as the VAC/IE regimen). The first set of drugs includes vincristine, doxorubicin (Adriamycin), and cyclophosphamide. After the patient recovers from the effects of these drugs, another combination of drugs, ifosfamide and etoposide, is given. Some doctors may use slightly different combinations of drugs.

Chemotherapy is given for at least 12 to 24 weeks before surgery or radiation to the tumor and is then given afterward as well. Usually a total of about 14 to 15 cycles of chemo are given, which can take from about 6 months to close to a year to complete, depending on the schedule. If the tumor has spread, these same drugs may be given at higher doses.

Soon after the Ewing tumor is diagnosed (but before starting chemotherapy), the doctor may suggest inserting a venous access device into a large vein in the patient’s chest. The device is a catheter (hollow tube) that is inserted surgically while the patient is under general anesthesia (asleep). One end of the catheter stays in the vein, while the other end lies just under or outside the skin. This lets the healthcare team give chemo and other drugs and to draw blood samples without having to stick needles into the veins each time. The device can usually remain in place for several months, and can make having chemotherapy less painful. If such a device is used in your child, the healthcare team will teach you how to care for it to reduce the risk of problems such as infections.

Possible side effects of chemotherapy

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 chemotherapy, which can lead to side effects.

Children tend to have less severe side effects from chemo than adults and often recover from side effects more quickly. This is why doctors can often give them higher doses of chemotherapy to kill the tumor.

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are taken.

General side effects: Side effects common to many chemo drugs include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea
- 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 are short-term and tend to go away after treatment is finished. There are often ways to lessen these side effects. For example, you can be given drugs to help prevent or reduce nausea and vomiting, or to help get blood cell counts back to normal levels. Be sure to discuss any questions you have about side effects with the cancer care team.

Side effects of certain drugs: Along with the effects listed above, certain chemo drugs can have specific side effects.

Cyclophosphamide and ifosfamide can damage the bladder, which can cause blood in the urine. The risk of this happening can be lowered by giving the drugs with plenty of fluids and with a drug called *mesna*, which helps protect the bladder. These drugs can also damage the ovaries or testicles, which might affect fertility (the ability to have children) when children reach young adulthood.

Doxorubicin can cause heart damage. This risk goes up as the total amount of the drug that is given goes up. Doctors try to limit this risk as much as possible by not giving more than the

recommended doses of doxorubicin and by checking the heart with a test called an echocardiogram during treatment.

Vincristine can damage nerves. Some patients may notice tingling and numbness, particularly in the hands and feet. This often goes away or gets better once treatment is stopped, but it may be long lasting in some people.

Some drugs used to treat Ewing tumors, such as etoposide, can increase the risk of later developing a cancer of white blood cells known as *acute myeloid leukemi*a. Fortunately, this doesn't happen often.

Long-term or late side effects: Some side effects may not go away or may not happen until years after treatment is finished. Examples include:

- Infertility (being unable to have children)
- Heart damage
- Developing a second cancer

Some of these long-term effects are described in the section, "What happens after treatment for Ewing tumors?"

Tests to check for side effects of chemotherapy: Before each chemotherapy treatment, your (child's) doctor will check lab test results to be sure the liver, kidney, and bone marrow are functioning well. If not, chemotherapy may need to be delayed or the doses reduced.

The complete blood count (CBC) includes counts of white blood cells, red blood cells, and blood platelets. Chemotherapy can lower the numbers of these blood cells, so blood counts will be watched closely during and after chemotherapy. The cells usually reach their lowest point about 2 weeks after chemo is given, though this can occur earlier with high-dose regimens.

Blood chemistry tests measure certain chemicals in the blood that tell doctors how well the liver and the kidneys are working. Some chemo drugs can damage the kidneys and liver.

If doxorubicin (Adriamycin) is to be given, tests such as an echocardiogram (an ultrasound of the heart) may be done to check heart function before and during treatment.

For more information on chemotherapy, see our document, *Understanding Chemotherapy: A Guide for Patients and Families*.

Surgery for Ewing tumors

Several types of surgery can be used for Ewing tumors. The choice depends on the tumor's size and location, and how surgery would change the function of the affected part of the body.

Many tumors in soft tissues and certain bones can be removed without causing major disability or deformity. Other tumors, such as those in most bones of the arms and legs, cannot be completely removed without affecting the limb's function.

Tumors in the arms or legs

For most tumors in an arm or leg, a limb-sparing operation can remove part or all of the affected bone while leaving the arm or leg basically intact. The bone that is removed is replaced either with a bone graft (piece of bone from another part of the body or from another person) or with an internal prosthesis (a rod-shaped device made of metal and other materials that replaces part or all of a bone).

If the tumor is in the upper part of the leg, the femur (upper leg bone), including the knee, can be removed. It is replaced with a prosthesis for the bone and knee, which is connected to the lower leg. Tumors in the lower part of the leg are harder to treat this way, because it is harder to remove and reconstruct parts of the lower leg. The humerus (upper arm bone) is also suitable for limb-sparing surgery.

Limb-sparing surgery is a very complex operation. The surgeons who do this type of operation must have special skills and experience. The challenge for the surgeon is to be sure to remove the entire tumor while still saving the nearby tendons, nerves, and blood vessels to keep as much of the limb's function and appearance as possible. But if a cancer has grown into these structures, they will need to be removed along with the tumor. In such cases, radiation therapy or amputation may sometimes be the best option to treat the tumor.

Using an internal prosthesis in a growing child is especially challenging. In the past, it often required several operations over time to replace the prosthesis with a longer one as the child grew. Newer prostheses have become very sophisticated. Some can be made longer without any extra surgery. They have tiny devices in them that can lengthen the prosthesis when needed to make room for a child's growth. But even so, they may need to be replaced with an adult prosthesis once the child's body stops growing.

It takes about a year, on average, for patients to learn to walk after limb-sparing surgery on a leg. If the patient does not take part in the rehabilitation program, the salvaged arm or leg may become useless.

Some children may not be able to have limb-sparing surgery because their tumors are in parts of bones that are hard to replace or because the tumors also extend into vital nerves or blood vessels that cannot be removed without severely damaging the limb. These children usually get radiation therapy instead of surgery. In rare cases, amputating the affected limb may be the best option.

Tumors in the chest wall or pelvis (hip bones)

For a Ewing tumor in the chest wall, the surgeon often must remove the diseased area and also remove nearby ribs. The ribs are then replaced with a man-made material. If the child's tumor has spread to the lungs, the chest can be opened and the lung tumors can be removed during an operation called a *thoracotomy*. Often radiation therapy to the chest is also given to these children.

Pelvic tumors can be hard to treat with surgery, and in many cases radiation therapy may be the preferred treatment. But if the tumor responds well to initial chemotherapy, surgery (sometimes followed by radiation therapy) may be an option. Pelvic bones can often be reconstructed after surgery.

Possible side effects of surgery

The short-term side effects of surgery can include poor wound healing, bleeding at the surgery site, and infection. Complications of limb-sparing surgery can include grafts or rods that become loose or broken. These complications are more likely than with surgery done for other reasons because chemotherapy or radiation therapy used before and after surgery can impair wound healing.

Rehabilitation after surgery: This might be the hardest part of treatment, and this discussion cannot describe this completely. Patients and parents must meet with a rehabilitation specialist to understand all of their options.

If a limb is amputated, the patient must learn to live with and use a prosthetic limb. This can be particularly hard for growing children if the prosthetic limb needs changing to keep up with their growth.

When only the tumor and part of the bone is removed in a limb-sparing operation, the situation can be even more complicated, especially in growing children. Children who have had limb-sparing surgery may need more surgery in the coming years to replace the internal prosthesis with one more suited to their growing body size, and some may eventually need an amputation.

Both amputation and limb-sparing surgery can have pros and cons. For example, limb-sparing surgery, although often more acceptable than amputation, tends to lead to more complications because of its complexity. Growing children who have limb-sparing surgery are also more likely to need further surgery down the road.

When researchers have looked at the final results of the different surgeries in terms of quality of life, there has been little difference between them. Perhaps the biggest problem has been for teens, who may worry about the social effects of their operation. Emotional issues can be very important, and support and encouragement are needed for all patients.

For more information on surgery as a treatment for cancer, see our document, *Understanding Cancer Surgery: A Guide for Patients and Families.*

Radiation therapy for Ewing tumors

Radiation therapy focuses high-energy beams in the tumor from a machine outside the body to kill the cancer cells. In people with Ewing tumors, radiation therapy may be used with surgery, or it may be used instead of surgery, especially if it would be hard to remove the entire tumor. In either case, chemotherapy is usually given before, during, and afterward.

This type of treatment is given by a doctor called a *radiation oncologist*. Before treatments start, the radiation team takes careful measurements with imaging tests such as MRI scans to determine the correct angles for aiming the beams and the proper dose of radiation.

Most often, radiation treatments are given 5 days a week for several weeks. Each treatment is much like getting an x-ray, but the dose of radiation is much higher. The treatment is not painful. For each session, your child will lie on a special table while a machine delivers the radiation from a precise angle.

Each treatment lasts only a few minutes, but the setup time – getting your child into place for treatment – usually takes longer. Some younger children may be given medicine to make them drowsy before each treatment.

Some newer techniques allow doctors to focus the radiation more precisely:

Three-dimensional conformal radiation therapy (3D-CRT): Three-dimensional CRT uses the results of imaging tests such as MRI and special computers to precisely map the location of the tumor. Several radiation beams are then shaped and aimed at the tumor from different directions. Each beam alone is fairly weak, which makes it less likely to damage normal body tissues, but the beams converge at the tumor to give a higher dose of radiation there. Your child may be fitted with a plastic mold resembling a body cast to keep him or her in the same position during each treatment so that the radiation can be aimed more accurately.

Intensity modulated radiation therapy (IMRT): IMRT is an advanced form of 3D therapy that may be especially useful for tumors near the spine. Along with shaping the beams and aiming them at the tumor from several angles, the intensity (strength) of the beams is adjusted to limit the dose reaching the most sensitive normal tissues. This lets the doctor deliver a higher dose to the tumor. Many major hospitals and cancer centers now use IMRT, especially for tumors in hard-to-treat areas such as the spine or pelvis (hip bones).

Conformal proton beam radiation therapy: Proton beam therapy is related to 3D-CRT and uses a similar approach. But instead of using x-rays like most other techniques, it focuses proton beams on the tumor. Protons are positive parts of atoms. Unlike x-rays, 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. Doctors can use

this property to deliver more radiation to the tumor and do less damage to nearby normal tissues.

As with IMRT, this approach may be helpful for hard-to-treat tumors, such as those on the spine or pelvic bones. The machines needed to make protons are expensive, and there are only a handful of them being used in the United States at this time.

Possible side effects of radiation therapy

Because of the possible side effects of radiation therapy (especially in growing children), surgery is often preferred if it is possible. But improvements in the way radiation therapy is given now allow children with Ewing tumors to be treated with lower doses than were used in the past, helping to reduce some of these side effects.

The side effects of radiation therapy depend on the dose of radiation and where it is aimed. Some effects may be short term, while others may have a longer lasting impact.

Short-term problems include effects on skin areas that receive radiation, which can range from mild sunburn-like changes and hair loss to more severe skin reactions. Radiation to the abdomen or pelvis can cause nausea, diarrhea, and urinary problems.

Long-term side effects can be more serious, especially in growing children, so doctors try to limit them as much as possible.

A serious problem of radiation therapy in children is that it can affect bone growth. In younger children, some bones will not grow well after radiation. For example, radiation to the bones in one leg may result in it being much shorter than the other. Radiation of facial bones may cause uneven growth, which might affect how a child looks. But if a child is fully or almost fully grown, this is less likely to be an issue.

Depending on where the radiation is aimed, it can also damage other organs:

- Radiation to the chest wall or lungs can affect lung and heart function.
- Radiation to the pelvis can damage the bladder or intestines, which can lead to problems with urination or bowel movements. It can also damage reproductive organs, which could affect fertility later in life, so doctors do their best to protect these organs by shielding them from the radiation or moving them out of the way whenever possible.
- Side effects of radiation therapy to the spinal cord or brain may include nerve damage, headaches, and trouble thinking, which usually become most serious 1 or 2 years after treatment. Fortunately, Ewing tumors rarely spread to the brain, but they can sometimes extend into the brain from nearby bones of the skull.

Another major concern with radiation therapy is that it may cause a new cancer to form in the part of the body that was treated with the radiation. This is most often a different type of bone cancer called *osteosarcoma*. The higher the dose of radiation, the more likely this is to

occur. This small risk should not keep children who need radiation from getting treatment. Still, it's important to continue follow-up visits with your child's doctor so that if problems come up they can be found and treated as early as possible.

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

High-dose chemotherapy and stem cell transplant for Ewing tumors

This type of treatment is being studied for use in patients with Ewing tumors that are hard to cure with other treatments, such as those with metastatic disease or with Ewing tumors that come back after the standard treatment.

The doses of chemotherapy drugs that can be given safely are normally limited by the side effects these drugs can cause. One of the most concerning side effects is damage to the bone marrow, which is where new blood cells are made. Even though higher doses of these drugs might be more effective in treating Ewing tumors, they can't be given because they would severely damage bone marrow cells, leading to life-threatening shortages of blood cells.

To try to get around this problem, a doctor may treat the child with high-dose chemotherapy and then use a stem cell transplant to "rescue" the bone marrow, giving the child new blood stem cells to replace those destroyed by the chemotherapy.

In the past, this type of treatment was often called a *bone marrow transplant*.

If a stem cell transplant is considered as part of the initial treatment plan for a Ewing tumor, the patient first gets standard doses of chemotherapy, then local treatment of the tumor (surgery and/or radiation therapy), followed by high-dose chemotherapy and a stem cell transplant.

What happens in a stem cell transplant

The first step in a stem cell transplant is to collect, or harvest, the child's own blood-producing stem cells to use later. (These are the cells that make the different types of blood cells.) This type of transplant, where the stem cells are taken from the patient (as opposed to coming from someone else), is known as an *autologous transplant*.

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

Once the stem cells have been frozen and stored, the child gets high-dose chemotherapy, sometimes along with radiation therapy. When the treatment is finished, the patient's stem cells are thawed and returned to the body in a blood transfusion. The stem cells travel through the bloodstream and settle in the bone marrow. Over the next 3 or 4 weeks, they start to make new, healthy 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 blood 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 antibiotics may also be used to prevent or treat infections or bleeding problems.

Practical points

A stem cell transplant is a complex treatment that can cause life-threatening side effects because of the high doses of chemotherapy used. If the doctors think your child may benefit from a transplant, it should be done at a nationally recognized cancer center where the staff has experience in doing the procedure and managing the recovery period.

A stem cell transplant often requires a long hospital stay and can be very expensive (costing well over $100,000). Because the procedure is so expensive, you should 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 tens of thousands of dollars. It is 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

Possible early complications and side effects are basically those caused by the high-dose chemotherapy (see the "Chemotherapy" section of this document), and can be severe. They result from damage to the bone marrow and other quickly dividing tissues of the body, and 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 infection. 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.

Some complications and side effects can last for a long time or may not occur until 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 information on stem cell transplants, see our document, *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants).*

Clinical trials for Ewing tumors

You may have had to make a lot of decisions since you've been told you (or your child) has a Ewing tumor. One of the most important decisions you will make is deciding which treatment is best. You may 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 get a closer look at promising new treatments or procedures.

If you would like to find out more about clinical trials you (or your child) may be eligible for, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical 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 Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials website at www.cancer.gov/clinicaltrials.

People have to meet certain requirements to take part in any clinical trial. If you (or your child) qualify for a clinical trial, you will have to decide whether or not to enter (enroll) in it. Older children, who can understand more, usually must also agree to take part in the clinical trial before the parents' consent is accepted.

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

You can get a lot more information on clinical trials in our document, *Clinical Trials: What You Need to Know*. You can read it on our website or call our toll-free number (1-800-227-2345) and have it sent to you.

Complementary and alternative therapies for Ewing tumors

You might hear about ways to treat cancer or relieve symptoms that are different from mainstream (standard) medical treatment. Everyone from friends and family to Internet 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 pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you (or your child) may lose the chance to be helped by standard medical treatment. Delays or interruptions in medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer (or with children who have 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 of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for “red flags” that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to use regular medical treatments? Is the treatment a “secret” that requires you to take your child to certain providers or to another country?
- Talk to your (child’s) doctor or nurse about any method you are thinking about.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at.

The choice is yours

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

Treatment of Ewing tumors by stage

Treatment of a Ewing tumor is based mainly on its location and how much it has spread when first found.

Localized Ewing tumors

As mentioned earlier, even children with localized Ewing tumors may still have cancer spread to other parts of the body that is too small to be seen with imaging tests. If these children do not get chemotherapy, these small pockets of cancer cells would eventually become larger tumors. This is why chemotherapy, which can reach all parts of the body, is an important part of treatment for localized Ewing tumors.

Once the Ewing tumor has been diagnosed and staged, the first treatment is chemotherapy. It is called *neoadjuvant* chemotherapy because it is given before any surgery or radiation therapy. In the United States, treatment is usually a regimen known as VAC/IE, which is a combination of vincristine, doxorubicin (Adriamycin), and cyclophosphamide, alternated with ifosfamide and etoposide, although other combinations of the same drugs are also effective.

After at least 12 weeks of chemotherapy, imaging tests such as CT, MRI, PET, or bone scans are done to see if the tumor is shrinking and can be surgically removed.

If so, surgery is done at this point. If cancer cells are found at or near the edges of the surgery specimen (meaning cancer cells may have been left behind), radiation therapy and chemotherapy (for several months) are used. If there are no cancer cells at or near the edges of the surgery specimen, chemotherapy may be used without radiation therapy.

If the tumor is not growing but surgery is not an option after the initial chemotherapy, radiation therapy (along with chemotherapy) is usually the next treatment given. In some cases this may shrink the tumor enough so that surgery can then be done. This would then be followed by more chemotherapy, possibly with more radiation as well. In other cases where surgery is still not an option, radiation therapy and chemotherapy are the main treatments.

If the Ewing tumor continues to grow despite the initial chemotherapy, a second type of chemotherapy (using different drugs) may be tried. Surgery or radiation therapy may also be tried to help keep the tumor under control. This may be followed by more chemotherapy.

Metastatic Ewing tumors

Patients who clearly have metastatic disease when they are first diagnosed are harder to treat than patients with localized disease. The outlook is better when the cancer has only spread to the lungs, as opposed to when the cancer has spread to other bones or to the bone marrow.

Treating metastatic disease is similar in many ways to treating localized disease. Chemotherapy is the first treatment, often using a more intense regimen than would be used if the cancer was localized. After a few months, tests such as CT or MRI scans, bone or PET scans, and/or bone marrow biopsies are done to see how the cancer has responded to treatment.

If the cancer has only spread to a few small areas, the main (primary) tumor and all known areas of metastases may be removed with surgery at this point. Other options, such as surgery plus radiation therapy (before and/or after surgery) or radiation therapy alone to all known metastatic sites, including the lungs, might also be tried. During and after these treatments, chemotherapy is given for several months as well.

Doctors at several cancer centers are now studying giving very intensive chemotherapy followed by a stem cell transplant to try to improve the outcome for these patients. For more on this procedure, see the “High-dose chemotherapy and stem cell transplant” section of this document.

Because these tumors can be hard to treat, clinical trials of newer treatments may be a good option in many cases.

Ewing tumors that recur (come back) after treatment

Recurrence of Ewing tumors after treatment is less likely now than in the past, but it can happen. If the tumor does recur, treatment may depend on a number of factors, including:

- The size and location of the tumor
- Whether it has spread to different parts of the body
- What types of treatment were used before

- How long it has been since treatment

Chemotherapy, surgery, radiation therapy, or some combination of these may be used to treat recurrent tumors, depending on the situation. Doctors are also studying the use of high-dose chemotherapy followed by a stem cell transplant and the use of targeted drugs such as monoclonal antibodies, but it is not yet clear how useful these are. These tumors can be hard to treat, so clinical trials of newer treatments may be a good option.

Social, emotional, and other issues in treating Ewing tumors

Most Ewing tumors develop during the teenage years, a very sensitive time in a young person's life. A diagnosis of a Ewing tumor and its treatment can have a profound effect on a person's outward appearance and how they view themselves and their body. It can also affect some everyday tasks and certain school, work, or recreational activities. The effects are often greatest during the first year of treatment. It's important that the treating center assess the family situation as soon as possible, so that any areas of concern can be addressed.

Some common family concerns include financial stresses, traveling to and staying near the cancer center, the possible loss of a job, and the need for home schooling. Many experts recommend that school-aged patients attend school as much as possible. This can help them maintain a sense of daily routine and keep their friends informed about what is happening.

Friends can be a great source of support, but patients and parents should know that some people have misunderstandings and fears about cancer. Some cancer centers have a school re-entry program that can help in these situations. In this program, health educators visit the school and inform students about the diagnosis, treatment, and changes that the cancer patient may go through. They also answer any questions from teachers and classmates. (For more information, see our separate document, *Children Diagnosed With Cancer: Returning to School*.)

Centers that treat many patients with Ewing tumors may have programs to introduce new patients to children or teens who have finished their treatment. This can give patients an idea of what to expect during and after treatment, which is very important. Seeing another patient with a Ewing tumor doing well can also be a source of inspiration. There are also support groups that encourage athletics and full use of the child's limbs. Many amputees or people with prostheses are able to take part in athletics and often do.

Although the psychological impact of this disease in children and teenagers is most obvious, adults with this disease face many of the same challenges. They should also be encouraged to take advantage of the cancer centers' physical therapy, occupational therapy, and counseling services.

More treatment information for Ewing tumors

For more details on treatment options – including some that may not be addressed in this document – other good sources of information include the National Cancer Institute (NCI) and the National Comprehensive Cancer Network (NCCN).

The NCI provides treatment information by phone (1-800-4-CANCER) and on its website (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. These are available on the NCCN website (www.nccn.org). Treatment guidelines for Ewing tumors of bone are included in the "Bone Cancer" guidelines.

What should you ask the doctor about Ewing tumors?

It is important to have frank, open discussions with your cancer care team. They want to answer all of your questions, no matter how minor they might seem. For instance, consider these questions:

- What kind of Ewing tumor do I (does my child) have?
- Has the cancer spread beyond the main (primary) site?
- What is the stage of the cancer and what does that mean?
- Do we need to have other tests done before we can decide on treatment?
- How much experience do you have treating this type of cancer?
- What other doctors will I (we) need to see?
- What are our treatment options?
- What do you recommend and why?
- How long will treatment last? What will it be like? Where will it be done?
- How will treatment affect our daily lives?
- What should I (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 may develop later on?

- How might treatment affect my child's ability to grow and develop?
- Are there fertility issues we need to consider?
- What are the chances of the cancer coming back after treatment? What will we do if this happens?
- What type of follow up and rehabilitation will be needed after treatment?
- Are there nearby support groups or other families who have been through this that we could talk to?

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 that you can plan your work or school schedules. Or you may want to ask about second opinions or about available clinical trials.

What happens after treatment for Ewing tumors?

Following treatment for a Ewing tumor, the main concerns for most families are the short- and long-term effects of the tumor and its treatment, and concerns about the tumor still being there or coming back.

It is 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 visits and tests

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

Physical exams, x-rays, and other imaging tests (CT, MRI, PET, and/or bone scans) are often done about every 2 to 3 months for the first 2 years following treatment, and then less often during the following years. If Ewing tumors come back, it is usually within the first 2 years after treatment, but they can sometimes come back even many years later, so continued follow-up visits are important.

Your child's doctors will also continue to watch for signs of side effects from treatment and monitor physical rehabilitation after treatment. Measurements of growth and blood tests may

be done. The chemotherapy drug doxorubicin (Adriamycin) can affect the heart, so tests to measure heart function (such as echocardiograms) will probably be done as well.

During this time, it is very important to report any new symptoms to the doctor right away so that any problems can be found early, when they can be treated most effectively.

Possible late and long-term effects of cancer treatment

More young people treated for cancer are now surviving into adulthood. Doctors have learned that the treatment might 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.

Treating cancer in young people requires a very specialized approach, and so does care and follow-up after treatment. The earlier problems are recognized, the more likely it is they can be treated effectively.

Young people with cancer are at risk, to some degree, for several possible late effects of their cancer treatment. This risk depends on a number of factors, such as the size and location of the cancer, the treatments received, doses of cancer treatment, and the patient's age when they are treated. For example, the after-effects of surgery for Ewing tumors may range from small scars to the loss of a limb, which would require both physical rehabilitation and emotional adjustment.

Other late effects of cancer treatment can include:

- Heart or lung problems (caused by certain chemotherapy drugs or radiation therapy to the chest)
- Slowed or decreased growth and development (in the bones or overall)
- Changes in sexual development and ability to have children (see below)
- Learning problems
- Development of second cancers (see below)

Infertility: Infertility is not a common side effect of treatment for Ewing tumors, but it can occur. Young women may have changes in menstrual periods during chemotherapy, but normal monthly cycles usually return after treatment ends. Boys and men may lose the ability to make sperm. This usually returns, but the sperm count might remain low. Radiation to the pelvis may also affect fertility.

Talk to your cancer care team about the risks of infertility with treatment, and ask if there are options for preserving fertility, such as sperm banking. For more information, see our document, *Fertility and Women With Cancer* or *Fertility and Men With Cancer*.

Second cancers: Children who are cured of their original cancers may be at higher risk for other cancers later in life. Some chemotherapy drugs used to treat Ewing tumors can cause leukemia in a small fraction of children later on. If this occurs, it is usually within 5 years after treatment. A concern in those treated with radiation therapy is the development of a new cancer (usually another type of bone cancer) at the site of treatment. These typically begin to develop about 5 years after radiation, and the risk remains higher for many years. Doctors are studying ways to reduce these risks while maintaining the effectiveness of current treatments. For more information on second cancers, see our document, *Second Cancers Caused by Cancer Treatment*.

Long-term follow-up care for childhood cancer survivors

To help increase awareness of late effects and improve follow-up care for 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 may be treated.

It is 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 download them for free at 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 review them with a doctor.

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

Keeping good medical records

As much as you may want to put the experience behind you once treatment is completed, it is very important to keep good records of your (child's) medical care during this time. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. This can be very helpful later on if you (or your child) change doctors. Be sure the doctors have the following information:

- A copy of the pathology report(s) from any biopsies or surgeries
- If there was surgery, a copy of the operative report(s)
- If you (your child) stayed in the hospital, copies of the discharge summaries that doctors prepare when patients are 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

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

What's new in Ewing tumor research and treatment?

Research on Ewing tumors is being done at many medical centers, university hospitals, and other institutions across the world.

Diagnosis

Scientists are developing new techniques to more accurately diagnose Ewing tumors. New lab tests of tumor samples (see the section "How are Ewing tumors diagnosed?") are being studied to see if they can help identify Ewing tumors and give more information on how well specific treatments might cure that particular tumor.

Treatment

Researchers are looking to develop better treatments for Ewing tumors, as well as to find less toxic treatments for those that can be cured.

Chemotherapy

The Children's Oncology Group, individual universities, and children's hospitals are studying new chemotherapy combinations, which often include newer drugs such as topotecan, irinotecan, temozolomide, gemcitabine, docetaxel, trabectedin, and mithramycin (plicamycin).

Doctors are also trying to make the currently used drugs more effective by changing the way they are given. For example, they have found that giving the standard VAC/IE chemo regimen more often – that is, every 2 weeks instead of every 3 weeks – seems to lower the chance of localized Ewing tumors coming back, without increasing the risk of serious side effects. This is often called *compressed chemotherapy*.

Researchers are also studying high-dose chemotherapy with stem cell transplants in those with Ewing tumors that are unlikely to be cured with current treatments.

Targeted therapy

As noted in the section “Do we know what causes Ewing tumors?”, great progress is being made in understanding the changes in genes and chromosomes that cause Ewing tumors to form.

This knowledge has already been used to develop very sensitive lab tests to detect this cancer, and doctors are now studying how to best use these tests to guide the choice of treatment. It might also lead to new drugs that target these changes in Ewing tumor cells.

Some new drugs that target specific changes in Ewing tumor cells are already being tested. For example, drugs that target the insulin-like growth factor receptor-1 (IGF-1R), a protein on some cancer cells that causes them to grow, are now being studied in clinical trials. Early studies have found that these drugs can shrink some Ewing tumors and slow down the growth of others. So far, this benefit has been temporary in most cases. Researchers continue to study these drugs and ways to combine them with other targeted drugs.

Other newer drugs being studied for use against Ewing tumors include:

- Drugs that affect a tumor’s ability to make new blood vessels, such as bevacizumab (Avastin)
- Drugs that target the mTOR protein, such as temsirolimus (Torisel) and everolimus (Afinitor)

Additional resources for Ewing tumors

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

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)

Nutrition for Children with Cancer (also available 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

Understanding Cancer Surgery: A Guide for Patients and Families (also in Spanish)

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

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

Clinical Trials: What You Need to Know

Fertility and Women With Cancer

Fertility and Men With Cancer

Second Cancers Caused by Cancer Treatment

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

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*

In addition to the American Cancer Society, other sources of patient 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.

Amputee Coalition of America
Toll-free number: 1-888-AMP-KNOW (1-888-267-5669)
Website: www.amputee-coalition.org

Offers resources for specific groups with amputations, including parents and youth (see their "Limb Loss Resource Center" online); also lists some local support groups across the country.

Children's Oncology Group
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.

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)
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.

National Dissemination Center for Children with Disabilities (NICHCY)
Toll-free number: 1-800-695-0285 (also for TTY)
Website: www.nichcy.org

Offers information about children and teens with disabilities, guides to dealing with schools, monthly e-newsletter, and referrals to other organizations as needed. Also available in Spanish.

Websites for teens and children

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

Web site has animated stories and interactive programs to teach kids about chemo and procedures that may be done in the hospital; also provides a safe, monitored online support group for teens with cancer.

Group Loop (a subsite of the Cancer Support Community just for teens)
Toll-free number: 1-888-793-9355
Website: www.grouploop.org

An online place for teens with cancer or teens who know someone with cancer to connect with other teens – away from the pressures of classes, responsibilities, and treatment schedules. Has online support groups, chat rooms, information, and more.

Teens Living with Cancer
Website: www.teenslivingwithcancer.org

An online-only resource dedicated to teens coping with a cancer diagnosis and treatment. It focuses on teen issues and provides resources to support teens, their families, and friends.

SuperSibs!
Toll-free number: 1-888-417-4704
Website: www.supersibs.org

Supports, honors, and recognizes 4- to 18-year-old 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.*

Other publications*

For adults

100 Questions & Answers About Your Child's Cancer, William L. Carroll and Jessica Reisman. Jones and Bartlett Publishers, 2004.

Cancer & Self-Help: Bridging the Troubled Waters of Childhood Illness, Mark A. Chester and Barbara K. Chesney. University of Wisconsin Press, 1995.

Care for Children and Adolescents with Cancer. National Cancer Institute, 2008. Available at: www.cancer.gov/cancertopics/factsheet/NCI/children-adolescents or call 1-800-422-6237.

Childhood Cancer: A Parent's Guide to Solid Tumor Cancers, 2nd ed. Honna Janes-Hodder and Nancy Keene. Childhood Cancer Guides, 2002.

Childhood Cancer: A Handbook from St Jude Children's Research Hospital, Grant Steen and Joseph Mirro (editors). Perseus Publishing, 2000.

Childhood Cancer Survivors: A Practical Guide to Your Future, Kathy Ruccione, Nancy Keene, and Wendy Hobbie. Childhood Cancer Guides, 2012.

Children with Cancer: A Comprehensive Reference Guide for Parents, Jeanne Munn Bracken. Oxford University Press, 2010.

Educating the Child With Cancer: A Guide for Parents and Teachers, edited by Nancy Keene. Candlelighters Childhood Cancer Foundation, 2003.

Living with Childhood Cancer: A Practical Guide to Help Families Cope, Leigh A. Woznick and Carol D. Goodheart. American Psychological Association, 2002.

Surviving Childhood Cancer: A Guide for Families, Margo Joan Fromer.New Harbinger Publications, 1998.

When Bad Things Happen to Good People, Harold Kushner. First Anchor, 2004.

When Someone You Love Is Being Treated for Cancer. National Cancer Institute, 2012. Available at: www.cancer.gov/cancertopics/coping/when-someone-you-love-is-treated, or call 1-800-422-6237.

Young People with Cancer: A Handbook for Parents. National Cancer Institute, 2003. Available at: www.cancer.gov/cancertopics/coping/youngpeople, or call 1-800-422-6237.

Your Child in the Hospital: A Practical Guide for Parents (2nd Edition), Nancy Keene and Rachel Prentice. O'Reilly & Associates. 1999. (Also available in Spanish.)

Books for teens and children

Although these books are intended for children, younger kids are helped more when an adult reads with and helps the child reflect about what different parts of the book mean to the child.

Chemo, Craziness and Comfort: My Book about Childhood Cancer, Nancy Keene. Candlelighters Childhood Cancer Foundation, 2002. For ages 6 to 12.

Childhood Cancer Survivors: A Practical Guide to Your Future, Kathy Ruccione, Nancy Keene, and Wendy Hobbie. Childhood Cancer Guides, 2012. For older teens.

Going to the Hospital, Fred Rogers. Paperstar Book, 1997. For ages 4 to 8.

Little Tree: A Story for Children with Serious Medical Problems, Joyce C. Mills. Magination Press, 2003. For ages 4 to 8.

Living Well With My Serious Illness, Marge Heegaard. Fairview Press, 2003. For ages 8 to 12.

My Book for Kids with Cansur [sic], Jason Gaes. Viking Penguin, 1998. For ages 4 to 8.

What About Me? When Brothers and Sisters Get Sick, Allan Peterkin and Frances Middendorf. Magination Press, 1992. For brothers and sisters (ages 4 to 8) of a child with cancer.

When Someone Has a Very Serious Illness: Children Can Learn to Cope with Loss and Change, Marge Heegaard. Woodland Press, 1991. For ages 6 to 12.

When Your Brother or Sister Has Cancer: A Guide for Teens, National Cancer Institute, 2011. Available at www.cancer.gov/cancertopics/coping/when-your-parent-has-cancer, or call 1-800-422-6237.

Why, Charlie Brown, Why? A Story About What Happens When a Friend Is Very Ill, Charles M. Schultz. Ballantine Publishing Group, 1990. For ages 6 to 12.

**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.

References: Ewing family of tumors detailed guide

American Cancer Society. *Cancer Facts & Figures 2014*. Atlanta, Ga: American Cancer Society; 2014.

American Joint Committee on Cancer. Bone. *AJCC Cancer Staging Manual*. 7th ed. New York: Springer-Verlag; 2010: 281–287.

Bacci G, Longhi A, Barbieri E, et al. Second malignancy in 597 patients with Ewing sarcoma of bone treated at a single institution with adjuvant and neoadjuvant chemotherapy between 1972 and 1999. *J Pediatr Hematol Oncol*. 2005;27:517–520.

Bernstein M, Kovar H, Paulussen M, et al. Ewing’s sarcoma family of tumors: Current management. *Oncologist*. 2006;11:503–519.

Dome JS, Rodriguez-Galindo C, Spunt SL, Santana VM. Pediatric solid tumors: Ewing’s sarcoma family tumors. In: Abeloff MD, Armitage JO, Niederhuber JE. Kastan MB,

McKenna WG, eds. *Abeloff's Clinical Oncology*. 4th ed. Philadelphia, Pa: Elsevier; 2008:2085–2091.

Gebhardt MC, Springfield D, Neff JR. Sarcomas of bone: Ewing's sarcoma. In: Abeloff MD, Armitage JO, Niederhuber JE. Kastan MB, McKenna WG, eds. *Abeloff's Clinical Oncology*. 4th ed. Philadelphia, Pa: Elsevier; 2008:1982–1994.

Gorlick R, Janeway K, Lessnick S, Randall RL, Marina N; COG Bone Tumor Committee. Children's Oncology Group's 2013 blueprint for research: Bone tumors. *Pediatr Blood Cancer*. 2013;60:1009–1015.

Grier HE, Krailo MD, Tarbell NJ, et al. Addition of ifosfamide and etoposide to standard chemotherapy for Ewing's sarcoma and primitive neuroectodermal tumor of bone. *New Engl J Med*. 2003; 348:694–701.

Hawkins DS, Bolling T, Dubois S, et al. Ewing sarcoma. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 6th ed. Philadelphia Pa: Lippincott Williams & Wilkins; 2011:987–1014.

Kolb EA, Kushner BH, Gorlick R, et al. Long-term event-free survival after intensive chemotherapy for Ewing's family of tumors in children and young adults. *J Clin Oncol*. 2003;21:3423–3430.

Lee J, Hoang BH, Ziogas A, Zell JA. Analysis of prognostic factors in Ewing sarcoma using a population-based cancer registry. *Cancer*. 2010;116:1964–1973.

Miser JS, Krailo MD, Tarbell NJ, et al. Treatment of metastatic Ewing's sarcoma or primitive neuroectodermal tumor of bone: Evaluation of combination ifosfamide and etoposide – A Children's Cancer Group and Pediatric Oncology Group study. *J Clin Oncol*. 2004;22:2873–2876.

Miser JS, Goldsby RE, Chen Z, et al. Treatment of metastatic Ewing sarcoma/primitive neuroectodermal tumor of bone: Evaluation of increasing the dose intensity of chemotherapy — A report from the Children's Oncology Group. *Pediatr Blood Cancer*. 2007;49:894–900.

Naing A, LoRusso P, Fu S, et al. Insulin growth factor-receptor (IGF-1R) antibody cixutumumab combined with the mTOR inhibitor temsirolimus in patients with refractory Ewing's sarcoma family tumors. *Clin Cancer Res*. 2012;18:2625–2631.

National Cancer Institute. Physician Data Query (PDQ). Ewing Sarcoma Treatment. 2012. Accessed at www.cancer.gov/cancertopics/pdq/treatment/ewings/healthprofessional on April 10, 2013.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Bone Cancer. Version 2.2013. Accessed at www.nccn.org/professionals/physician_gls/pdf/bone.pdf on April 10, 2013.

Rodriguez-Galindo C. Pharmacological management of Ewing sarcoma family of tumours. *Expert Opin Pharmacother*. 2004;5:1257–1270.

Rodriguez-Galindo C, Liu T, Krasin MJ, et al. Analysis of prognostic factors in Ewing sarcoma family of tumors: Review of St. Jude Children's Research Hospital studies. *Cancer*. 2007;110:375–384.

Russell HV, Pappo AS, Nuchtern JG, et al. Solid tumors of childhood: Ewing's sarcoma. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 8th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2008:2061–2067.

Subbiah V, Anderson P. Targeted therapy of Ewing's sarcoma. *Sarcoma*. 2011;2011:686985. Epub 2010 Oct 31.

Toomey EC, Schiffman JD, Lessnick SL. Recent advances in the molecular pathogenesis of Ewing's sarcoma. *Oncogene*. 2010;29:4504–4516.

Womer RB, West DC, Krailo MD, et al. Randomized controlled trial of interval-compressed chemotherapy for the treatment of localized Ewing sarcoma: A report from the Children's Oncology Group. *J Clin Oncol*. 2012;30:4148–4154.

Last Medical Review: 6/12/2013
Last Revised: 2/4/2014

For additional assistance please contact your American Cancer Society
1-800-227-2345 or www.cancer.org