



## EWING FAMILY OF TUMORS - ALL SECTIONS

### What is cancer?

The body is made up of hundreds of millions of living cells. Normal body cells grow, divide, 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. 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 most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

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 for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. 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 different from the types that develop in adults. Although there are exceptions, childhood cancers tend to respond better to chemotherapy. Children also tolerate chemotherapy better than adults. But chemotherapy can have some long-term side effects, and children who survive their cancer will need careful attention for the rest of their lives.

Since the 1960s, most children and adolescents with cancer have been treated at specialized centers designed for them. Being treated in specialized centers offers them 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, pathologists, surgeons, radiation oncologists, 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 experienced experts.

## 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 tissue that share some common features. They can occur 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
- extrasosseous Ewing tumor (EOE)
- peripheral primitive neuroectodermal tumor (PPNET)

### **Ewing sarcoma of bone**

Ewing sarcoma, the most common of the tumors in this family, is a type of bone tumor that occurs most often in children. It was first described by Dr. James Ewing in 1921, who found it was different from the more common bone tumor, osteosarcoma. It is more likely to respond to radiation, and its cells look different when viewed under a microscope.

### **Extrasosseous Ewing tumor**

Extrasosseous Ewing (EOE) tumors start in soft tissues around bones, but they look and act very much like Ewing sarcomas in bones. They are also known as extraskelatal Ewing sarcomas.

### **Peripheral primitive neuroectodermal tumor**

This rare childhood cancer also starts in the bone or soft tissue and shares many features with Ewing tumor 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 the separate American Cancer Society 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 have the same DNA abnormalities and share similar proteins, which are rarely found in other types of cancers. Because of this, it is believed that these 3 cancers develop from the same type of normal cells in the body. Although there are slight differences among these tumors, they are all treated in the same way.

Most Ewing tumors occur in the bones. The most common sites are the pelvis, 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.

## What are the key statistics about Ewing tumors?

Only about 1% to 2% of all childhood tumors are Ewing tumors. About 250 children and adolescents are diagnosed with Ewing tumors in the United States each year.

About 2 out of 3 of these cancers occur in those between ages 10 and 20. Ewing tumors can also affect adults into their 20s and 30s as well as children under 10.

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 are discussed in the section "How are Ewing tumors staged?"

## 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. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancers of the lung, mouth, larynx (voice box), bladder, kidney, and several other organs.

But risk factors don't tell us everything. Having a risk factor, or even several, does not mean that a person will get the disease, and many people get cancer without having any known risk factors.

Unlike many adult cancers, lifestyle-related risk factors do not seem to play a large 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 Ewing tumors are known (see "Do we know what causes Ewing tumors?"), they are not inherited.

## **Race/ethnicity**

Ewing tumors occur most often in whites and are extremely rare among African Americans and Asian Americans. The reason for this is not known.

## **Gender**

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

## **Age**

Although these tumors can occur at any age, they are most common in teenagers and are rare among adults and young children.

## **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 contain instructions for controlling when our cells grow, divide, and die. Certain genes that speed up cell division are called *oncogenes*. Others that slow down cell division, or cause cells to die at the right time, are called *tumor suppressor genes*. Cancers can be caused by DNA mutations (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 apparent reason.

In about 85% of cases, the change is a swapping of genetic material between chromosomes 22 and 11. Less frequently, the swapping occurs between chromosomes 22 and 21, or rarely between 22 and another chromosome. This swapping is called a *translocation*. The result of this translocation is to move 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. The activation of the EWS gene leads to overgrowth of the cells and to the development of this cancer, although 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 "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.

## **Can Ewing tumors be prevented?**

Although many adult cancers can be prevented by lifestyle changes that reduce certain risk factors, at this time there are no known ways to prevent Ewing tumors or most other cancers in children.

## **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, in some cases Ewing tumors are found early, before they have spread widely.

The most common symptom of a Ewing tumor is pain in the area of the tumor. 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 and not feel well.

Of course, children and teens may get sore or have lumps and bumps from normal activities. But pains or lumps that stay around for a long time should be checked by a doctor. The same is true if a lump feels warm and/or the child has a fever. The lump is more likely to be caused by an infection, but this also needs to be seen by a doctor right away.

## **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**

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 tissue covering the bone (periosteum), or the pain may be from a break or a fracture of a bone that has been weakened by the tumor.

Most Ewing bone tumors and almost all of the non-bone Ewing tumors (of soft tissue) 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 noticeable until the tumor has grown quite large.

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 or paralysis, 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 evaluated and treated, if needed.

Because many of these signs and symptoms are also typical of 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 condition does not quickly go away or does not improve with antibiotics, at which time the bone is x-rayed.

## **Medical history and physical exam**

If your child has signs or symptoms that may suggest a tumor, the doctor will want to take a complete medical history to check for symptoms. A physical exam can provide information about the tumor and other health problems. For example, the doctor may be able to see or feel an abnormal mass.

If symptoms and/or the results of the physical exam suggest a Ewing tumor (or other tumor) might be present, more involved tests will probably be done. These might include imaging tests, biopsies, and/or lab tests.

## **Imaging tests**

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

- to help find out if a suspicious area might be cancerous
- to learn how far cancer may have spread
- to help determine if treatment has been effective

Most patients who have or may have cancer 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, the doctor will probably order an x-ray. A radiologist (doctor who specializes in reading imaging tests) can usually identify a bone tumor on an x-ray and can often recognize 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 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 a mass seen on an x-ray. MRI scans can usually tell if the mass 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 important when planning surgery or radiation therapy. MRI is also useful in seeing the effect of the treatment on the tumor.

MRI scans provide detailed images of soft tissues in the body. But MRI scans use 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 of parts of the body. 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 to have done. 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 are often used to see if a Ewing tumor has spread to the lungs, lymph nodes, or liver.

The CT scan is an x-ray test that produces detailed cross-sectional images of parts of the body. 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. Unlike a regular x-ray, a CT scan creates detailed images of the soft tissues in the body.

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 the 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. Your child will need to lie still on a table while they are being done. During the test, the table moves in and out of the scanner, a ring-shaped machine that completely surrounds the table. Some people feel a bit confined by the ring they have to lie in 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.

*Spiral CT* (also known as helical CT) is now available in many medical centers. This type of CT scan uses a faster machine. The scanner part of the machine rotates around the body continuously, allowing doctors to collect the images much more quickly than with a standard CT. This lowers the chance of blurred images occurring as a result of breathing motion. It also lowers the dose of radiation received during the test. The image slices are also thinner, which yields more detailed pictures.

### **Bone scan**

A bone scan can help show if a cancer has metastasized (spread) to the bones, and is often part of the workup for children with a Ewing tumor. This test is useful because it provides a picture of the entire skeleton at once.

For this test, a small amount of low-level radioactive material is injected into a vein (intravenously, or IV). 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 make an accurate diagnosis, other imaging 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, glucose (a form of sugar) that contains a radioactive atom is injected into the blood. The amount of radioactivity used is very low. Because cancer cells in the body are growing quickly, they absorb large amounts of the radioactive sugar. A special camera can then create 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, in finding out whether abnormal areas seen on a bone scan or CT scan are tumors, and also in following the response to treatment.

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 with the more detailed appearance of that area on the CT.

## **Biopsy of the tumor**

Although the results of imaging tests may strongly suggest that cancer is present, 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.* Proper planning of the biopsy location and technique can 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 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**

If the tumor is large or cannot be easily removed, 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). Although incisional biopsies in adults are sometimes done using a local anesthetic (numbing medicine), 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 procedures 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 lumps when the child is still asleep. The doctor may also do a bone marrow biopsy (see below) to see if the cancer has spread to other bones.

During the biopsy (while the child is still asleep), a pathologist can take a quick look at the tissue sample under the microscope. If it is a Ewing tumor, the surgeon may place a central venous access 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 vein. This is better for the child when chemotherapy is given at a later time because they will get fewer needle sticks. (See the discussion on chemotherapy in the section, "How are Ewing tumors treated?").

## **Bone marrow aspiration and biopsy**

These tests look 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 is cleaned, the skin over the hip 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 for pain or 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 will be 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 pathologist (a doctor specializing in using lab tests to diagnose diseases) looks at all biopsy specimens under a microscope to see if cancer is present. In most cases, the specific type of cancer can 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 sample is treated with special proteins (antibodies) that specifically attach to substances that are 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 (long strands of DNA) are looked at under a microscope to detect any changes. As noted in the section "Do we know what causes Ewing tumors?", cells from Ewing tumors usually have chromosome translocations, where 2 chromosomes swap pieces of their DNA. In most cases, Ewing tumor cells have translocations between chromosomes 11 and 22. Less often, the translocation is between chromosome 22 and another chromosome. Finding these changes can help distinguish Ewing tumors from other types of cancer.

Standard cytogenetic testing usually takes about 3 weeks because the cancer cells must grow in lab dishes for a couple of weeks before their chromosomes can be seen under the microscope. A newer form of cytogenetic testing is called *fluorescence in situ hybridization (FISH)*. FISH uses special fluorescent dyes to recognize specific chromosome changes in Ewing tumors. FISH is very accurate and can usually provide results within a couple of days, which is why this test is now used in many medical centers.

### **Reverse transcription polymerase chain reaction (RT-PCR)**

This test is another way to find translocations in the Ewing family of tumors cells to confirm the type of tumor. Instead of using a microscope to look for the chromosome changes as in cytogenetic testing, RT-PCR uses chemical analysis of the RNA (a substance related to DNA) from genes affected by the translocation. RT-PCR testing is often able to find translocations that aren't 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 a translocation, it is likely that the cancer has not been cured and more treatment may be needed.

### **Blood tests**

There are no blood tests that can be used to diagnose the Ewing family of tumors. But certain blood tests may be helpful once a diagnosis has been made.

A complete blood count (CBC) can show abnormal levels of white blood cells, red blood cells, and platelets in the blood. An abnormal CBC result 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 has been linked with a larger amount of tumor in the body, which indicates the cancer may be harder to treat.

Blood tests can also be done to check a child's general health (especially before surgery) and to look for side effects during treatment such as chemotherapy. These tests may include complete blood counts and tests to measure how well the liver and kidneys are working.

## How are Ewing tumors staged?

Staging is the process of finding out how far a cancer has spread. The outlook (prognosis) for people with cancer depends, to a large extent, on the cancer's stage. The stage of a cancer is one of the most important factors in choosing treatment.

The stage of a Ewing tumor 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?"

## AJCC staging system for bone cancer

A staging system is a standardized way in which the cancer care team describes the extent of the cancer. The American Joint Committee on Cancer (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. Extrasosseous 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 that are important in fighting infections). 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 is a description of how the cells 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.

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: No evidence of the 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 multiple sites 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 lung

M1b: The cancer has spread to other sites

### **Grades of bone cancer**

G1-G2: Low grade

G3-G4: High grade

(All Ewing tumors are considered to be 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:** The tumor is confined to the bone, is 8 cm across or less, and is low grade.

## **Stage IB**

**T2 or T3, N0, M0, G1 to G2:** The tumor is confined to the bone, is either larger than 8 cm across (T2) or it is in more than one place on the same bone (T3). It is low grade.

## **Stage IIA**

**T1, N0, M0, G3 to G4:** The tumor is confined to the bone, is 8 cm across or less, and is high grade.

## **Stage IIB**

**T2, N0, M0, G3 to G4:** The tumor is confined to the bone, is larger than 8 cm across, and is high grade.

## **Stage III**

**T3, N0, M0, G3 or G4:** The tumor is confined to the bone but has "skipped" to other sites in the same bone. It is high grade.)

## **Stage IVA**

**Any T, N0, M1a, any G:** The tumor has spread only to the lungs. (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 lung. It can be any size or grade.

## **Localized vs. metastatic stages**

In practice, doctors rely on 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 include 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/or 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), which is why chemotherapy is an important part of treatment for 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, the spread is to the lungs or to other bones or the bone marrow. Less common sites of spread include the liver and 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 found by imaging tests.

### **Survival rates by stage**

Survival rates are often used by doctors to produce a standard way of discussing a person's prognosis (outlook). 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. These numbers are based on people treated several years ago. Improvements in treatment since then will probably result in a more favorable outlook for patients now being diagnosed with Ewing tumors.

Survival statistics can sometimes be useful as a general guide, but they may not accurately represent any one person's prognosis. Other factors (such as those below) may also affect outlook. Your child's doctor is likely to be a good source as to whether these numbers may apply to your case, as he or she is familiar with the aspects of the particular situation.

### **Localized tumors**

With modern treatment, the 5-year survival rate for patients with a localized Ewing tumor is around 70%.

### **Metastatic tumors**

When metastases are present at diagnosis, the 5-year survival rate is about 20% 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 located on an arm or leg (as opposed to pelvis)
- normal blood LDH level
- good tumor response to chemotherapy
- age younger than 10

## **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**

The goals of treatment of the Ewing family of tumors are:

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

To achieve these goals, a team approach involving many specialists is needed. Surgeons, pediatric oncologists, radiation oncologists, pathologists, psychosocial specialists, and rehabilitation specialists work together to give children and adolescents the best treatment and quality of life possible. This can be best done at a children's cancer center that is a member of the Children's Oncology Group.

Most patients with the Ewing family of 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 the Ewing family of tumors have come from the results of these clinical trials.

The types of treatment used in Ewing tumors include surgery, chemotherapy, and radiation therapy. In almost all cases, both chemotherapy and localized therapy (surgery and/or radiation therapy) is needed.

The rest of this section describes the types of treatment used for Ewing tumors and when these treatments are used in different situations.

## **Surgery**

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 body part.

Many of the tumors in soft tissues and certain bones can be removed without causing major disability or deformity. Others, 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**

In most cases, limb-sparing operations can be done to remove portions of a bone and replace it with a bone graft (piece of bone from another part of the body or from another person) or with a metal and/or plastic prosthesis. Sometimes, an entire bone can be replaced with a prosthesis. A prosthesis that replaces an arm or leg bone can sometimes cause problems in a growing child, but some newer models can be lengthened as the child grows, which can reduce the need for future surgeries.

If the tumor is in the upper part of the leg, the femur (upper leg bone), including the knee, can be removed. A prosthesis for the bone and knee can then be placed to connect to the lower leg. It is harder to remove and reconstruct the lower leg. The humerus (upper arm bone) is also suitable for limb-sparing surgery because it does not support the weight of the body.

Limb-sparing surgery is complex and can be done only by specially trained surgeons. A child may need more operations and months of physical therapy before the affected limb functions well.

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**

If a child has a Ewing tumor in the chest wall, the surgeon often must remove the diseased area and also remove ribs. The ribs are replaced with a man-made material to close the chest wall defect. If the child's tumor has spread to the lungs, the chest can be opened and the lung tumors can be removed. This operation is 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. Bone grafts may not always fuse well to existing bone, and bone fractures are possible. Complications are more likely than with surgery done for other reasons because chemotherapy or radiation therapy used before and after surgery may interfere with wound healing.

After surgery, many children will need physical rehabilitation. Physical and occupational therapists often work with patients to get the best possible outcome. Depending on the age of the child and how a limb is reconstructed, further surgery may be needed as the child grows. Even then, some children may have permanent limb deformities.

For more information on surgery as a treatment for cancer, see the separate American Cancer Society document, *Surgery*.

## **Chemotherapy**

Chemotherapy 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 reach all areas of the body. This is part of treatment for just about all children with Ewing tumors.

As noted in "How are Ewing tumors staged?" children with localized Ewing tumors have no metastases apparent in bone marrow specimens or on imaging tests. However, many children with localized Ewing tumors still have metastases that are too small to be seen with these tests. If these children do not receive chemotherapy, these small metastases would eventually develop into larger tumors.

A combination of several chemotherapy drugs is used to treat children with Ewing tumors. In the United States, the most common regimen is to alternate between 2 combinations of drugs given every 2 to 3 weeks. The first combination of drugs includes vincristine, doxorubicin (Adriamycin), and cyclophosphamide. In some cases, a fourth drug, dactinomycin, may be added as well. After the child recovers from the effects of these drugs, another combination of drugs, ifosfamide and etoposide, is given.

The 2- to 3-week cycles are given for 12 to 16 weeks before surgery or radiation to the tumor and are then given afterward as well (usually for a total of 14 to 15 cycles). If the tumor has spread, these same drugs may be given at higher doses.

Soon after the Ewing tumor is diagnosed, the doctor may suggest inserting a venous access device into a large vein in the child's chest. The device is a catheter (hollow tube) that is inserted surgically while the child 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 allows the health care team to give drugs into the blood system 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 much less painful for the child. If such a device is used in your child, the health care team will teach you how to care for it to reduce the risk of problems such as infections.

### **Possible side effects of chemotherapy**

Chemotherapy drugs work by attacking 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, 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 seem to have an advantage over adults when it comes to chemotherapy. They tend to have less severe side effects and recover from side effects more quickly. One benefit of this is that doctors can give the high doses of chemotherapy necessary 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 of chemotherapy drugs can include:

- hair loss
- mouth sores
- loss of appetite
- nausea and vomiting
- increased chance of infections (due to low white blood cell counts)
- easy bruising or bleeding (due to low blood platelet counts)
- fatigue (due to low red blood cell counts)

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, drugs can be given to help prevent or reduce nausea and vomiting. Be sure to discuss any questions you have about side effects with the cancer care team.

Along with the effects listed above, certain medicines have specific side effects.

Cyclophosphamide and ifosfamide can damage the bladder. This can be avoided or minimized by giving the drugs with plenty of fluids and with a drug called mesna, which helps protect the bladder. These drugs can also cause changes in the menstrual cycle, and can damage the ovaries or testicles, which might affect fertility (the ability to have children).

Doxorubicin can cause heart damage. Doctors try to reduce 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.

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 leukemia. Fortunately, this doesn't happen often.

For more information on chemotherapy, see the separate American Cancer Society document, *Understanding Chemotherapy: A Guide for Patients and Families*.

## **Radiation therapy**

Radiation therapy uses high-energy radiation to kill 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 surgically. In either case, chemotherapy is usually given before, during, and afterward.

External beam radiation therapy focuses high-energy beams on the cancer from a machine outside the body. This is the type of radiation therapy most often used to treat Ewing tumors.

Before treatments start, the radiation team takes careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. External radiation therapy is much like getting an x-ray, but the radiation is more intense. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time -- getting your child into place for treatment -- usually takes longer. Most often, radiation treatments are given 5 days a week for several weeks.

Some newer external radiation 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 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 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. In addition to shaping the beams and aiming them at the tumor from several angles, the intensity (strength) of the beams can be adjusted to limit the dose reaching the most sensitive normal tissues. This may let doctor deliver a higher dose to the tumor. Many major hospitals and cancer centers are now able to provide IMRT.

### **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 is given now allow children with Ewing tumors to be treated with less radiation than was 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.

Effects on skin areas that receive radiation can range from mild sunburn-like changes to more severe skin reactions. Radiation to the abdomen or pelvis can cause nausea, diarrhea, and urinary problems. In some cases there may be significant long-term damage to the bladder or bowel.

A serious problem of radiation therapy in children is that it can interfere with bone growth. In younger children, some bones will not grow well after radiation. For example, one leg may be much shorter than the other. Radiotherapy of facial bones may cause uneven growth, and some disfigurement may result. If a child is fully or almost fully grown, however, the side effects of radiation therapy will not be as severe.

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.

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 extend into the brain from nearby bones of the skull.

For more detailed information on radiation therapy, see the separate American Cancer Society document, *Understanding Radiation Therapy: A Guide for Patients and Families*.

## **High-dose chemotherapy and stem cell transplant**

This type of treatment is being studied for use in patients with Ewing tumors that are unlikely to be cured with other treatments, such as patients with metastatic disease or those whose disease comes back after the standard treatment. It involves giving very high doses of chemotherapy, and then replacing the body's bone marrow cells, which were killed by the treatment. When this approach is used, the patient receives the standard chemotherapy first, and then receives high-dose chemotherapy and a stem cell transplant. In the past, this type of treatment was commonly referred to as a bone marrow transplant.

The bone marrow is the soft tissue in the middle of some bones where new red blood cells, white blood cells, and platelets are formed. Red blood cells carry oxygen to all parts of the body. White blood cells are part of the immune system, which fights off infections. Platelets are needed to help the blood clot to stop bleeding.

The usual doses of chemotherapy drugs can affect quickly dividing cells like those in the bone marrow. Even though higher doses of these drugs might be more effective in treating tumors, they can't be given because they would 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 give a peripheral blood stem cell transplant (PBSCT) to "rescue" the bone marrow.

### **What happens in a peripheral blood stem cell transplant**

The first step in a PBSCT 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 taken from the child's bone marrow, which required a minor operation. But doctors have found that these cells can be taken from the bloodstream using a procedure known as apheresis. This is similar to donating blood, but 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.

Once the stem cells have been 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 process similar to a normal blood transfusion. The stem cells travel through the bloodstream and settle in the bones. Over the next 3 or 4 weeks, they start to make new, healthy blood cells in the child's bone marrow.

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

### **Practical points**

A peripheral blood stem cell transplant is a complex treatment. If the doctors think your child may benefit from a transplant, the best place to have this done is at a nationally recognized cancer center where the staff has experience in doing the procedure and managing the recovery period.

A stem cell transplant is also very expensive (often costing more than \$100,000) and often requires a lengthy hospital stay. Because the procedure is so expensive, you should have an idea of how the costs might be covered beforehand. Be sure to get written approval from your insurer if the procedure is recommended for your child.

### **Possible side effects**

Possible early complications and side effects are basically the same as those caused by any other type of high-dose chemotherapy (see the "Chemotherapy" section of this document), and are caused by damage to the bone marrow and other quickly dividing tissues of the body. They can include low blood cell counts (with increased risk of infection and bleeding), nausea, vomiting, loss of appetite, mouth sores, and 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. Be sure to talk to your child's doctor before the transplant to learn about possible long-term effects your child may have.

For more information on stem cell transplants, see the separate American Cancer Society document, *Bone Marrow & Peripheral Blood Stem Cell Transplants*.

## Clinical trials

You may have had to make a lot of decisions since you've been told your child has cancer. 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 your child to take part in a clinical trial, 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 Web site at <http://clinicaltrials.cancer.org>. 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 Web site at [www.cancer.gov/clinicaltrials](http://www.cancer.gov/clinicaltrials).

Your child will have to meet certain requirements to take part in any clinical trial. If your infant or young child does qualify for a clinical trial, you will have to decide whether or not to enter (enroll) the child into 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 for your child. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for every child.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our Web site or call our toll-free number and have it sent to you.

## Complementary and alternative therapies

When your child has cancer you are likely to hear about ways to treat his or her cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites 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 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 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 parents who have children with cancer think about alternative methods. You want to do all you can to help fight the cancer, and the idea of a treatment with 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 child's 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 how your child is treated. If you want to use a non-standard treatment, learn all you can about the method and talk to your child's doctor about it. With good information and the support of your child's health care team, you may be able to safely use the methods that can help your child while avoiding those that could be harmful.

## **Treatment of Ewing tumors by stage**

## **Localized Ewing tumors**

After the Ewing tumor is diagnosed, the first treatment is chemotherapy. It is called *neoadjuvant* chemotherapy because it is given before any surgery or radiation therapy. As already described, treatment is usually a combination of vincristine, doxorubicin, and cyclophosphamide, alternated with ifosfamide and etoposide, although other combinations of the same drugs are also effective.

After at least 8 to 12 weeks of chemotherapy, imaging tests such as CT, MRI, PET, or bone scans are done to see if the tumor can be surgically removed. If so, surgery is done at this point. If surgery is not an option or if after the operation cancer cells are found at the edges of the surgery specimen (meaning cancer cells may have been left behind), radiation therapy is used. In either case, this is typically followed by more chemotherapy, which is given for several more months. Chemotherapy is not interrupted during radiation therapy.

## **Metastatic Ewing tumors**

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

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 primary tumor and all known areas of metastases may be removed at this point. Other options, such as surgery plus radiation therapy or radiation therapy alone to all known metastatic sites, including the lungs, might also be tried.

After treatment to control the primary tumor, chemotherapy is given again for several months.

To improve the outcome for these patients, an approach consisting of very intensive chemotherapy followed by a peripheral blood stem cell transplant is being studied at several cancer centers. For more information 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 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 the child had before
- how long it has been since treatment

Chemotherapy, surgery, and radiation therapy may be used to treat recurrent tumors. Doctors are also studying the use of high-dose chemotherapy followed by a peripheral blood stem cell transplant, although it is not yet clear how useful this is. Because treatment of these tumors can be difficult, clinical trials of newer treatments may be a good option.

## **Psychosocial considerations in treating Ewing tumors**

Most cases of the Ewing family of tumors develop during the teenage years, a very sensitive time in a child's life. A diagnosis of a Ewing tumor can greatly affect a patient's ability to continue certain school, work, or recreational activities. The impact is greatest during the first year of treatment. The treatment center should evaluate the patient's family situation as soon as possible. If the patient or family members have any concerns, these can be addressed early to avoid a crisis.

Some common family concerns include financial stresses, transportation to 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 helps patients maintain important social connections and gives them a chance to tell their friends what is happening to them.

Friends can be a great source of support, but patients 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 will go through. They also answer any questions from teachers and classmates.

Centers that treat many patients with Ewing tumors may have programs to introduce new patients to children or adolescents who have finished their treatment. Seeing another patient with a Ewing tumor doing well is often the best inspiration for a patient.

## **More treatment information**

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

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site ([www.cancer.gov](http://www.cancer.gov)). Detailed guidelines intended for use by cancer care professionals are also available on [www.cancer.gov](http://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. Those are available on the NCCN Web site ([www.nccn.org](http://www.nccn.org)).

## **What should you ask your child's doctor about Ewing tumors?**

It is important to have frank, open discussions with your child's 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 does my child have?
- Has the cancer spread beyond the primary site?
- What is the stage of the cancer and what does that mean?
- Are there other tests that need to be done before we can decide on treatment?
- How much experience do you have treating this disease?
- What treatment options do we have?
- What do you recommend and why?
- How long will treatment last? What will it involve? Where will it be done?
- How will treatment affect our daily lives?
- What should we do to be ready for treatment?
- What are the possible short and long-term side effects of the suggested treatments?
- Are there fertility issues we need to consider?
- What are the chances of recurrence with these treatment plans? What would we do if this happens?
- What type of follow up and rehabilitation will my child need after treatment?

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 child's school schedule. Or you may want to ask about second opinions or about clinical trials for which your child may qualify.

## **What happens after treatment for Ewing tumors?**

Following treatment for a Ewing tumor, the main concerns for most families are the immediate and long-term effects of the tumor and its treatment, and concerns about the possibility of the tumor coming back.

It is certainly normal to want to put the tumor and its treatment behind you and to get back to your normal life. 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. Doctor visits and tests to look for signs that the cancer has come back are done more frequently 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.

Your child's doctors will also continue to watch for signs of side effects from treatment. Measurements of growth and blood tests may be done. Because the chemotherapy drug doxorubicin (Adriamycin) may affect the heart, 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 long-term effects of cancer treatment**

More children treated for cancer are now surviving into adulthood. With childhood cancer survivors living longer, in recent years more attention has been focused on their adult health status. Researchers have learned that childhood cancer treatment may affect that child's health later in life.

Just as the treatment of childhood cancer requires a very specialized approach, so does aftercare and monitoring for any late effects of treatment. Careful follow-up allows for early recognition of and attention to the after-effects of treatment.

Childhood cancer survivors 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 specific cancer treatments received, dosages of cancer treatment, and the child's age at the time of treatment. 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 (due to certain chemotherapy drugs or radiation therapy)
- slowed or decreased growth and development (in the bones or overall)
- changes in sexual development and ability to have children
- changes in intellectual function with learning problems
- development of second cancers (see below)

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. For more information on these and other possible late effects, please see our document, *Childhood Cancer: Late Effects of Cancer Treatment*.

**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. This usually occurs within 5 years after treatment. Another concern in those treated for Ewing tumors is the development of a new cancer (usually another type of bone cancer) at the site of radiation therapy. 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.

### **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. Eventually, your child will grow up, be on his or her own, and have new doctors. It is important that he or she be able to give the new doctors the exact details of the cancer diagnosis and treatment. Gathering the details soon after treatment may be easier than trying to get them at some point in the future. There are certain pieces of information that your child's doctors should have, even into adulthood. These include:

- a copy of the pathology report from any biopsies or surgeries
- if there was surgery, a copy of the operative report
- if there were hospitalizations, copies of the discharge summaries that doctors prepare when patients are sent home
- if there was chemotherapy treatment for the cancer, a list of the drugs, drug doses, and when they were given
- if there was radiation, a summary of the type and dose of radiation and when and where it was given

## **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 nation.

## **Diagnosis**

Scientists are developing new techniques to more accurately diagnose Ewing tumors. New lab tests of tumor samples (see "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.

## **Chemotherapy**

Most children with Ewing tumors respond to chemotherapy, radiation, and surgery. However, more work is needed to develop successful treatments for recurrent or metastatic Ewing tumors, as well as to find less toxic treatments for those that can be cured. 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, and trabectedin.

Researchers are also studying high-dose chemotherapy with peripheral blood 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.

More research on genetic changes in Ewing tumors could lead to new drugs that target the protein that appears to be responsible for this family of tumors, or to gene therapy (treatment with DNA to replace the damaged genes in Ewing tumor cells).

Some new drugs that target specific changes in Ewing tumor cells are already being tested. For example, several 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.

Bevacizumab (Avastin) is a targeted drug that slows growth of the blood vessels that provide nourishment to tumors. Bevacizumab is already used to treat some common forms of cancer,

including colorectal, breast, and lung cancer, and clinical trials are currently being done to see if it is also active against Ewing tumors.

## **Additional resources**

### **More information from your American Cancer Society**

We have selected some related information that may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

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

Because Someone I Love Has Cancer

Bone Marrow & Peripheral Blood Stem Cell Transplants

Childhood Cancer: Late Effects of Cancer Treatment

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

Children Diagnosed With Cancer: Financial and Insurance Issues

Children Diagnosed With Cancer: Returning to School

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

Closing the Umbrella: When Your Child's Treatment Ends

Family Medical Leave Act (FMLA)

Nutrition for Children With Cancer (also available in Spanish)

Pediatric Cancer Centers (also available in Spanish)

Surgery (also available in Spanish)

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

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

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

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

The following books are available from the American Cancer Society. Call us at 1-800-227-2345 to ask about costs or to place your order.

*Angels & Monsters: A Child's Eye View of Cancer* (for adults and teens)

*Because...Someone I Love Has Cancer* (kids' activity book)

*Caregiving: A Step-By-Step Resource for Caring for the Person with Cancer at Home*

*Jacob has Cancer: His Friends Want to Help* (coloring book for a child with a friend who has cancer)

## **National organizations and Web sites\***

In addition to the American Cancer Society, other sources of patient information and support include:

### **Candlelighters Childhood Cancer Foundation**

Toll-free number: 1-800-366-CCCF (1-800-366-2223)

Web site: [www.candlelighters.org](http://www.candlelighters.org)

### **National Cancer Institute**

Toll-free number: 1-800-4-CANCER (1-800-422-6237)

Web site: [www.cancer.gov](http://www.cancer.gov)

### **CureSearch (National Childhood Cancer Foundation and Children's Oncology Group)**

Toll-free number: 1-800-458-6223

Web site: [www.curesearch.org](http://www.curesearch.org)

### **National Children's Cancer Society, Inc.**

Toll-free number: 1-800-5-FAMILY (1-800-532-6459)

Web site: [www.children-cancer.org](http://www.children-cancer.org)

### **National Dissemination Center for Children with Disabilities (NICHCY)**

Toll-free number: 1-800-695-0285 (also for TTY)

Web site: [www.nichcy.org](http://www.nichcy.org)

### **Starlight Children's Foundation**

Telephone number: 1-310-479-1212

Web site: [www.starlight.org](http://www.starlight.org)

## **Teens Living with Cancer**

Web site: [www.teenslivingwithcancer.org](http://www.teenslivingwithcancer.org)

*\*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: Questions and Answers*. National Cancer Institute. Available at: [www.cancer.gov/cancertopics/factsheet/NCI/children-adolescents](http://www.cancer.gov/cancertopics/factsheet/NCI/children-adolescents) or call 1-800-332-8615.

*Childhood Cancer: A Parent's Guide to Solid Tumor Cancers*, Honna Janes-Hodder and Nancy Keene. O'Reilly and Associates, 1999.

*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*, Nancy Keene, Wendy Hobbie, and Kathy Ruccione. O'Reilly and Associates, 2000.

*Children with Cancer: A Comprehensive Reference Guide for Parents* (2nd Edition), Jeanne Munn Bracken and Pruden Pruden. Oxford University Press, 2005.

*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. G.K. Hall, 1982.

*When Someone You Love Is Being Treated for Cancer.* National Cancer Institute. Available at: [www.cancer.gov/cancertopics/when-someone-you-love-is-treated](http://www.cancer.gov/cancertopics/when-someone-you-love-is-treated), or call 1-800-332-8615.

*Young People with Cancer: A Handbook for Parents.* National Cancer Institute, 2003. Available at: [www.cancer.gov/cancertopics/youngpeople](http://www.cancer.gov/cancertopics/youngpeople), or call 1-800-332-8615.

*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.

*The Amazing Hannah, Look at Everything I Can Do!* Amy Klett. Candlelighters Childhood Cancer Foundation, 2002. For ages 1 to 6. (Also available in Spanish.)

*Chemo, Crazyness and Comfort: My Book about Childhood Cancer,* Nancy Keene. Candlelighters Childhood Cancer Foundation, 2002. Can be ordered from [www.candlelighters.org](http://www.candlelighters.org). For ages 6 to 12.

*Childhood Cancer Survivors: A Practical Guide to Your Future* (2nd Edition), Kathy Ruccione, Nancy Keene, and Wendy Hobbie. Patient Centered Guides, 2006. For older teens.

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

*Life Isn't Always A Day at the Beach: A Book for All Children Whose Lives Are Affected by Cancer*, Pam Ganz. High-Five Publishing, 1996. Workbook for ages 6 to 10.

*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. Ages 8 to 12.

*Me and My Marrow,* Karen Crowe. Fujsawa Healthcare, 1999. You can buy it as a book, but it's also available online at: [www.meandmy marrow.com/book/toc\\_ie.htm](http://www.meandmy marrow.com/book/toc_ie.htm). For teens.

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

*Oncology, Stupology...I Want to go Home!* Marilyn K. Hershey. Butterfly Press, 1999. For ages 8 to 12. (Also available in Spanish.)

*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.

*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.

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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](http://www.cancer.org).

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