



Ewing Family of Tumors

What is the Ewing family of tumors?

Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas of the body. To learn more about how cancers start and spread, see *What Is Cancer?* For information about the differences between childhood cancers and adult cancers, see *Cancer in Children*.

The Ewing family of tumors is a group of cancers that start in the bones or nearby soft tissues that share some common features. These tumors can develop at any age, but they are most common in the early teen years.

The main types of Ewing tumors are:

- **Ewing sarcoma of bone:** Ewing sarcoma that starts in a 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. Seen under a microscope, its cells looked different from osteosarcoma cells. 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 *extraskkeletal* Ewing sarcomas.
- **Peripheral primitive neuroectodermal tumor (PPNET):** This rare childhood cancer also starts in 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 *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)
- 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 the Ewing family of 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.**

Other types of bone cancers

Several other types of cancers can start in the bones.

Osteosarcomas are the most common bone cancer in children and teens. They are described in *Osteosarcoma*.

Most other types of bone cancers are usually found in adults and are rare in children. These include:

- Chondrosarcoma (cancer that develops from cartilage)
- Malignant fibrous histiocytoma
- Fibrosarcoma
- Chordoma
- Malignant giant cell tumor of bone

For more information on these cancers, see *Bone Cancer*.

Many types of cancer that start in other organs of the body can spread to the bones. These are sometimes referred to as *metastatic bone cancers*, but they are not true bone cancers. For example, if a rhabdomyosarcoma (a cancer that starts in muscle cells) spreads to the bones, it is still rhabdomyosarcoma and is treated like rhabdomyosarcoma. For more information, see *Bone Metastasis*.

The rest of this document refers only to Ewing tumors.

What are the key statistics about Ewing tumors?

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 younger children, as well as adults (mainly in their 20s and 30s).

Slightly more males than females develop these cancers. These tumors are much more common among whites, 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.”

Visit the American Cancer Society’s Cancer Statistics Center for more key statistics.

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 are much more common among 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. Genes that help cells grow, divide, or stay alive are called *oncogenes*. Others that slow down cell division or make cells die at the right time are called *tumor suppressor genes*. Cancers can be caused by changes in the cell's DNA 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 a single cell after a child is born, for unknown reasons.

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 chromosome 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 on tumor samples to look for translocations and confirm the diagnosis.

The gene changes that lead to Ewing tumors are now fairly well known, but it's still not clear what causes these changes. It might 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 at this time, nothing could have been 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) can't 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 often cause symptoms that allow them to be found early (before they have clearly spread to other parts of the body).

The most common symptom of a Ewing tumor is pain in the area of the tumor. Sometimes the tumor shows 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 sometimes the child has other 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.

Signs and symptoms of Ewing tumors

Ewing tumors are often found because of the symptoms they cause.

Pain

Most children and teens with Ewing tumors will have pain in the area of the tumor. Bone pain can be caused by the tumor spreading under the outer covering of the bone (periosteum), or the pain can be from a break (fracture) in 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 lump or swelling, which is more likely to be noticed in tumors in the arms or legs.

The lump is often soft and feels warm. Tumors in the chest wall or pelvis (hip bones) might not be noticed until they have grown quite large.

Other symptoms

Ewing tumors can also cause other symptoms, some of which are more common in tumors that have spread:

- Fever
- Feeling tired
- Weight loss

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 might not be recognized right away. For example, the doctor might try giving antibiotics first if an infection is suspected. The correct diagnosis might not be made until the signs and symptoms don't go away (or get worse) and the bone is then x-rayed.

How are Ewing tumors diagnosed?

Ewing tumors are usually found because of signs or symptoms a child or teen is having. If a tumor is suspected, tests will be needed to find out for sure.

Medical history and physical exam

If your child has signs or symptoms that could be from a tumor, the doctor will want to get a complete medical history to find out more about the symptoms 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 a doctor suspects the child might have a bone tumor (or another type of tumor), more tests will be done 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 can be done for many reasons, including:

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

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. 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 still 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 get a better look at an abnormal area seen on an x-ray. MRI scans usually can show 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 extent of a tumor, as they show in detail the marrow inside bones and the muscle, fat, and connective tissue around the tumor. Knowing 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 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 using radio waves and strong magnets instead of x-rays, so there is no radiation involved. A contrast material called *gadolinium* may be injected into a vein before the scan to help see details better.

MRI scans may take up to an hour. Your child may have to lie on a table that slides inside a narrow tube, which is confining and can be distressing. The test also requires a person to stay still for several minutes at a time. Open MRI machines, which are less confining, might be another option, but they still require 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 uses x-rays to make 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 can cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives. Rarely, more serious reactions like trouble breathing or low blood pressure can occur. Be sure to tell the doctor if your child has any allergies (especially to iodine or shellfish) or has ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays, but not as long as MRI scans. A CT scanner has been described as a large donut, with a narrow table that slides in and out of the middle opening. Your child will need to lie still on the table while the scan is being done. Some people feel a bit confined while the pictures are being taken, although it is not as narrow as an MRI tube. Some children 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 a bone scan might not be needed if a PET scan is done.)

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

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 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 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.

To learn more about these and other imaging tests, see our document *Imaging (Radiology) Tests*.

Biopsy of the tumor

The results of imaging tests might 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 is in a bone, it is very important that a surgeon experienced in treating bone tumors does the biopsy. Whenever possible, the biopsy and the surgery to treat the cancer should be planned together, and the same surgeon should do both. Proper planning of the biopsy can help prevent later complications and might reduce the amount of surgery needed later on.

There are a few 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. This can be done in a couple of ways:

- **Surgical (open) biopsy:** For this type of biopsy, the surgeon cuts away a piece of the tumor through an opening on the skin.
- **Needle (closed) biopsy:** In this type of biopsy, the surgeon puts a large, hollow needle through the skin and into the tumor to remove a piece of it.

Incisional biopsies are often done while the patient is under general anesthesia (in a deep sleep), but in older teens and adults they are sometimes done using sedation and a local anesthetic (numbing medicine).

If general anesthesia is going to be used 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 biopsy samples of these suspected tumors when the child is still asleep. The doctor might 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 lab tests to diagnose diseases) can take a quick look at the biopsy samples under a 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 large vein in the chest area during the same operation. The catheter end lies just under or outside on the skin. It can stay in place for several months during treatment. The catheter gives doctors and nurses easier access to the vein, which allows the child to get fewer needle sticks when chemotherapy is given or blood needs to be drawn at a later time.

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

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). The area over the hip is cleaned, and 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 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 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 cells are from a Ewing tumor.

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 almost always 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 can 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 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 leftover or recurrent cancer after treatment. For example, if RT-PCR testing of a bone marrow sample after treatment finds cells with a typical Ewing tumor translocation, it is likely that the cancer has not been cured, so more treatment is 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 a CBC 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 for the cancer care team to sum up 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 treatment purposes, doctors often use a

simpler system, dividing Ewing tumors into localized or metastatic groups. This is described below as well.

Staging can be confusing. If you have any questions about the stage of the cancer, ask someone on the health care team to explain it to you in a way you understand.

AJCC staging system for bone cancer

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 *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-sized 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. 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 after T, N, M, and G 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 can't be assessed

G1-G2: Low grade

G3-G4: High grade

(All Ewing tumors are considered G4.)

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 (T1) and is low grade (or the grade can't be assessed). The cancer has not spread to nearby lymph nodes (N0) or to distant parts of the body (M0).

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 (N0) or to distant parts of the body (M0).

Stage IIA

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

Stage IIB

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

Stage III

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

Stage IVA

Any T, N0, M1a, any G: The tumor has spread only to the lungs (M1a). 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 (N1). 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 (M1b). 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

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 (if done) do not find it has spread to other distant areas.

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 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.

When discussing cancer survival statistics, doctors often use a number called the *5-year survival rate*. 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 might result in a better 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 aren't a prediction of what will happen in any person's case. The stage of a person's cancer is important in estimating their outlook. But many other factors can also affect a person's prognosis, 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 when it is diagnosed, 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?

Treatment overview for Ewing tumors

Once a Ewing tumor has been found and staged, the cancer care team will talk with you about treatment options. It's important to be sure you understand your child's options as well as their possible side effects to help make the decision that's the best fit for your child. If there is anything you don't understand, ask to have it explained. You can find some good questions to ask in "What should you ask the doctor about 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 limit the long-term complications of treatment as much as possible

For children and teens, a team approach is recommended that includes the child's pediatrician as well as children's cancer specialists. Treatment for children and teens is best done at a children's cancer center. For adults with Ewing tumors, the treatment team typically includes the patient's primary care doctor, as well as specialists at a major cancer center. Doctors on the treatment team might include:

- An orthopedic surgeon (a surgeon who specializes in muscles and bones) who is experienced in treating bone tumors
- A medical or pediatric oncologist (a doctor who treats cancer with chemotherapy and other drugs)
- A radiation oncologist (a doctor who treats cancer with radiation therapy)
- A pathologist (a doctor specializing in lab tests to diagnose and classify diseases)
- A physiatrist (a doctor who directs a person's rehabilitation and physical therapy)

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

Before treatment, the doctors and other members of the team will help you, as a parent, understand the tests that will need to be done. The team's social worker will also counsel you about the problems you and your child might have during and after treatments such as surgery, and might be able to help you find housing and financial aid if needed.

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.

Your child's treatment will depend on the stage of the cancer and other factors. See "Treatment of Ewing tumors by stage" for information about the most common approaches.

Thinking about taking part in a clinical trial

Clinical trials are carefully controlled research studies that are done to get a closer look at promising new treatments or procedures. Clinical trials are one way to get state-of-the-art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

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.

If you would like to learn more about clinical trials that might be right for your child, start by asking your child's doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service at 1-800-303-5691 for a list of studies that meet your child's medical needs, or see the Clinical Trials section to learn more.

Considering complementary and alternative methods

You may hear about alternative or complementary methods that your doctor hasn't mentioned to treat your child's cancer or relieve symptoms. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

Complementary methods refer to treatments that are used along with regular medical care. Alternative treatments are used instead of a doctor's medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be dangerous.

Be sure to talk to your child's cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision. See the Complementary and Alternative Medicine section to learn more.

Help getting through cancer treatment

Your child's cancer care team will be your first source of information and support, but there are other resources for help when you need it. Hospital- or clinic-based support services are an important part of your child's care. These might include nursing or social work services, financial aid, nutritional advice, rehab, or spiritual help.

The American Cancer Society also has programs and services – including rides to treatment, lodging, support groups, and more – to help get through treatment. Call our National Cancer Information Center at 1-800-227-2345 and speak with one of our trained specialists on call 24 hours a day, every day.

The treatment information given here is not official policy of the American Cancer 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.

Chemotherapy for Ewing tumors

Chemotherapy (chemo) is the use of anti-cancer drugs delivered through a vein (IV) 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.

Chemo 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 chemo 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 found 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 (VAdriaC alternating with IE). 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 weeks before surgery or radiation 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 chemo), the doctor may suggest putting a catheter (a thin, soft tube) into a large vein in the patient’s chest. This is sometimes called a *venous access device* (VAD) or *central venous catheter* (CVC). The catheter is inserted surgically while the patient is under general anesthesia (in a deep sleep). 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 catheter usually stays in place for several months, and can make having chemo less painful. 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

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

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

The side effects of chemo 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 tend to go away after treatment is finished. There are often ways to lessen them. For example, drugs can be given 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.

Doxorubicin can damage the heart. This risk goes up as the total dose of the drug 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 chemo drugs can affect your (child's) ability to have children later in life. Talk to your (or your child's) cancer care team about the risks of infertility with treatment, and ask if there are options for preserving fertility, such as sperm banking or ovarian tissue banking.

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 on the possible late or long-term side effects of chemo, including infertility and second cancers, see “What happens after treatment for Ewing tumors?”

Tests to check for chemo side effects: Before each treatment, your (child's) doctor will check lab test results to be sure the liver, kidney, and bone marrow are working well. If not, chemo 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. Chemo can lower the numbers of these blood cells, so blood counts will be watched closely during and after chemo. The white blood cells and platelets 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 on chemotherapy, see the Chemotherapy section of our website, or *A Guide to Chemotherapy*.

Surgery for Ewing tumors

Surgery is an important part of treatment for virtually all Ewing tumors. It includes:

- The biopsy to diagnose the cancer
- The surgical treatment to remove the tumor(s)

Whenever possible, it's very important that the biopsy and surgical treatment be planned together, and that the same orthopedic surgeon at a cancer center does both the biopsy and the surgery to remove the tumor.

The main goal of surgery is to remove all of the cancer. If even a small number of cancer cells are left behind, they might grow and multiply to make a new tumor. To lower the risk of this happening, surgeons remove the tumor plus some of the normal tissue that surrounds it. This is known as *wide excision*.

Using a microscope, a pathologist will look at the removed tissue to see if the margins (outer edges) have cancer cells. If cancer cells are seen at the edges of the tissue, the margins are called *positive*. Positive margins can mean that some cancer was left behind. When no cancer cells are seen at the edges of the tissue, the margins are said to be *negative*, *clean*, or *clear*. A

wide excision with clean margins helps limit the risk that the cancer will grow back where it started.

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

Tumors in some soft tissues and certain bones can be removed without causing major disability or deformity. Other tumors, such as those in the bones of the arms and legs, often can't be removed completely without affecting the limb's function. Although all operations to remove Ewing sarcomas are complex, tumors in the arms or legs are generally not as hard to remove as those in other parts of the body, such as the base of the skull, the chest wall, the spine, or the pelvis (hip bones).

Tumors in the arms or legs

For most tumors in an arm or leg, surgery can remove part or all of the affected bone while leaving the arm or leg basically intact (a limb-sparing operation). 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. If the tumor has grown into these structures, they will need to be removed as well. 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 these prostheses may need to be replaced with a stronger adult prosthesis once the child's body stops growing.

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 can't 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 removed during an operation called a *thoracotomy*. Often these children also get radiation therapy to the chest.

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 sometimes be reconstructed after surgery, but in some cases pelvic bones and the leg they are attached to might need to be removed.

Possible side effects of surgery

Short-term risks and side effects: Surgery to remove a Ewing tumor is often a long and complex operation. Serious short-term side effects are not common, but they can include reactions to anesthesia, excess bleeding, blood clots, and infections. Pain is common after the operation, and the patient might need strong pain medicines for a while after surgery as the site heals.

Long-term side effects: The long-term side effects of surgery depend mainly on where the tumor is and what type of operation is done.

Complications of limb-sparing surgery can include bone grafts or prostheses that might become loose or broken. This is more likely than with surgery done for other reasons because chemo used before and after surgery can increase the risk of infection and affect wound healing. Infections are also a concern in people who have had amputations, especially of part of a leg, because the pressure placed on the skin at the site of the amputation can cause the skin to break down over time.

Rehabilitation after surgery: This might be the hardest part of treatment, and can't be described here completely. Patients and parents should meet with a rehabilitation specialist to understand all of their options.

Even when only the tumor and part of the bone is removed in a limb-sparing operation, the situation can still be 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.

It takes about a year, on average, for patients to learn to walk after limb-sparing surgery on a leg. Physical rehabilitation after limb-salvage surgery is extremely important. If the patient doesn't actively take part in the rehabilitation program, the salvaged arm or leg can become useless.

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. With proper physical therapy, patients are often able to walk on their own 3 to 6 months after a leg amputation.

Both limb-sparing surgery and amputation 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 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 all patients will need support and encouragement (see “Social, emotional, and other issues in treating Ewing tumors”).

Physical therapy and rehabilitation are very important for patients who have had surgery for Ewing tumors. Following the recommended rehab program offers the best chance for good long-term limb function. Even with proper rehab, people might still have to adjust to long-term issues such as changes in how they walk or do other tasks, and changes in appearance. Physical, occupational, and other therapies can often help people adjust and cope with these challenges.

For more on surgery as a treatment for cancer, see *A Guide to Cancer Surgery*.

Radiation therapy for Ewing tumors

Radiation therapy focuses high-energy beams at 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. Your child may be fitted with a plastic mold resembling a body cast to keep him or her in the same position each time so that the radiation can be aimed more accurately.

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 precise angles.

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 before each treatment to make them sleep so they won't move during treatment.

Some newer techniques let doctors 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.

Intensity modulated radiation therapy (IMRT): IMRT is an advanced form of 3D therapy that can 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. But instead of using x-rays, it focuses proton beams on the tumor. 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.

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 effect of radiation therapy in children is on 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 skull 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 on radiation therapy, see the Radiation Therapy section of our website or *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 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 (chemo) drugs that can be given safely are normally limited by the side effects these drugs can cause. One of the most serious 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 chemo (sometimes along with radiation therapy) and then use a stem cell transplant to “rescue” the bone marrow, giving the child new blood stem cells to replace those that were destroyed.

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 chemo, then local treatment of the tumor (surgery and/or radiation therapy), followed by high-dose chemo 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 chemo, 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 few 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. 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). Some insurance companies might view it as an experimental treatment and may not pay for it. Be sure to get a written approval from your insurer before treatment if

this procedure is recommended for your child. Even if the transplant is covered by your insurance, your co-pays or other costs could easily amount to many thousands of dollars. It 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

The possible side effects from a stem cell transplant are generally divided into early (short-term) and late (long-term) effects.

Early or short-term effects: Possible early complications and side effects are basically those caused by the high-dose chemo (see the Chemotherapy section of this document) and can be severe. They can include:

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

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

Late and long-term side effects: Some complications and side effects can last for a long time or might 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
- Cataracts (damage to the lens of the eye that can affect vision)
- Damage to bones or problems with bone growth
- Development of another cancer (including leukemia) years later

Be sure to talk to your child's doctor before the transplant to learn about possible long-term effects your child might have.

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

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 often 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 VAdriaC/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 can 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 might 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 “High-dose chemotherapy and stem cell transplant.”

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 depends 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, as well as the use of targeted drugs and immune therapies, 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

Social and emotional issues might come up both during and after treatment. Factors such as the person's age when diagnosed and the extent of treatment can play a role here.

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

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 *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 prosthetic limbs are able to take part in athletics and often do.

Parents and other family members can also be affected, both emotionally and in other ways. Some common family concerns during treatment include financial stresses, traveling to and staying near the cancer center, the possible loss of a job, and the need for home schooling. Social workers and other professionals at treatment centers can help families sort through these issues.

During treatment, patients and their families tend to focus on the daily aspects of getting through it and beating the cancer. But once treatment is finished, a number of emotional concerns can come up. Some of these might last a long time. They can include things like:

- Dealing with physical changes that can result from the treatment
- Worrying about the cancer returning or new health problems developing
- Feeling resentful for having had cancer or having to go through treatment when others do not

- Worrying about being treated differently or discriminated against (by friends, classmates, coworkers, employers, etc.)
- Being concerned about dating, marrying, and having a family later in life

No one chooses to have a Ewing tumor, but for many children and teens, the experience can eventually be positive, helping to establish strong self-values. Others may have a harder time recovering, adjusting to life after cancer, and moving on. It is normal to have some anxiety or other emotional reactions after treatment, but feeling overly worried, depressed, or angry can affect many parts of a young person's growth. It can get in the way of relationships, school, work, and other aspects of life.

With support from family, friends, other survivors, mental health professionals, and others, many people who have survived cancer can thrive in spite of the challenges they've had to face. If needed, doctors and other members of the health care team can often recommend special support programs and services to help after cancer treatment.

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

What should you ask the doctor about Ewing tumors?

It's 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?
- Will we need other tests before we can decide on treatment?
- How much experience do you have treating this type of cancer?
- Will I (we) need to see other doctors?
- What are our treatment options?
- What do you recommend and why?
- How soon do we need to start treatment?

- What should I (we) do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- How will treatment affect our daily lives?
- What are the risks and side effects of the suggested treatments?
- Which side effects start shortly after treatment and which ones might develop later on?
- Will treatment affect my child's ability to grow and develop?
- Will treatment affect my child's future ability to have children?
- What are the chances of the cancer coming back after treatment? What will we do if this happens?
- What type of follow up and rehab 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.

Also keep in mind that doctors are not the only ones who can provide you with information. Other health care professionals, such as nurses and social workers, may have the answers to some of your questions. You can find out more about speaking with your health care team in [*Talking With Your Doctor*](#).

What happens after treatment for Ewing tumors?

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

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

Follow-up 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's 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 every few months for the first couple of years following treatment, and then less often over time if there are no issues. 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.

Physical therapy and rehabilitation is typically a very important part of recovery after treatment, and your doctors and other health providers will continue to monitor your (child's) progress as time goes on.

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 can 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 chemo 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)

There may be other possible complications from treatment as well. Your child's doctor should carefully review any possible problems with you before your child starts treatment.

Along with physical side effects, some childhood cancer survivors might have emotional or psychological issues. They also may have problems with normal functioning and school work. These can often be addressed with support and encouragement. Doctors and other members of the health care team can also often recommend special support programs and services to help children after cancer treatment.

Fertility issues: Fertility problems are not common after treatment for Ewing tumors, but they 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 can also affect fertility.

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

Second cancers: Children who have been treated for Ewing tumors are 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.

The importance of treating the Ewing tumor generally far outweighs the small increased risk of getting another cancer. Still, doctors are studying ways to reduce these risks while maintaining the effectiveness of current treatments. For more information on second cancers, see *Second Cancers Caused by Cancer Treatment*.

Long-term follow-up care for children and teens

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 types of screening tests should be done to look for problems, and how late effects can be treated.

It's very important to discuss possible long-term complications with your child's health care team, and to make sure there is a plan in place to watch for these problems and treat them, if

needed. To learn more, ask your child's doctors about the COG survivor guidelines. You can also read them on the COG website: www.survivorshipguidelines.org. The guidelines are written for health care professionals. Patient versions of some of the guidelines are available (as "Health Links") on the site as well, but we urge you to discuss them with your doctor.

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

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. This can be very helpful later on if you (or your child) change doctors. Gathering these details during and soon after treatment may be easier than trying to get them at some point in the future. Be sure the doctors have the following information (and always keep copies for yourself):

- A copy of the pathology report(s) from any biopsies or surgeries
- Copies of imaging tests (CT or MRI scans, etc.), which can usually be stored digitally (on a DVD, etc.)
- 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's also very important to keep health insurance coverage. Tests and doctor visits cost a lot, and even though no one wants to think of the 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.

Understanding and diagnosing Ewing tumors

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 treatments might cure that particular tumor.

As researchers learn more about the changes inside Ewing tumor cells that make them different from normal cells, they hope to develop new treatments that take advantage of these changes (see below).

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 drugs such as topotecan, irinotecan, temozolomide, gemcitabine, docetaxel, 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 VAdriaC/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. These drugs may work best when combined with other 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)
- Drugs that target the PARP protein, such as olaparib and niraparib
- Drugs called HDAC inhibitors, such as vorinostat (Zolinza)

Immune therapy

A newer approach to treatment is to try to get the body's own immune system to recognize and attack the tumor cells. Some newer types of immune therapies have shown a great deal of promise in treating other types of cancer, and some of these approaches are now being looked at for Ewing tumors. These treatments are still in the early stages of testing at this time.

Additional resources for Ewing tumors

We have a lot more information that you might find helpful. Explore www.cancer.org or call our National Cancer Information Center toll-free number, 1-800-227-2345. We're here to help you any time, day or night.

National organizations and websites*

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

Websites for parents and adults

American Childhood Cancer Organization (formerly Candlelighters)

Toll-free number: 1-855-858-2226

Website: www.acco.org

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

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. Also has a searchable database to find the COG center closest to you.

CureSearch for Children's Cancer

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

Website: www.curesearch.org

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

National Cancer Institute

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

Website: www.cancer.gov

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

National Children's Cancer Society, Inc.

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

Website: www.children-cancer.org

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

Websites for teens and children**Starlight Children's Foundation**

Phone number: 1-310-479-1212

Website: www.starlight.org

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

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.

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.

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.*

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

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