Osteosarcoma

What are the differences between cancers in adults and children?

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

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

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

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

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

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

What is osteosarcoma?

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?*

Osteosarcoma (also called *osteogenic sarcoma*) is a type of cancer that starts in the bones. To understand osteosarcoma, it helps to know about bones and what they do.

About normal bones

Many people think of bones as just being part of the skeleton, like the steel girders that support a building. But bones actually do a number of different things.

- Some bones help support and protect our vital organs. Examples include the skull bones, breast bone (sternum), and ribs. These types of bones are often referred to as *flat bones*.
- Other bones, such as those in the arms and legs, make a framework for our muscles that helps us move. These are called *long bones*.
- Bones also make new blood cells. This is done in the soft, inner part of some bones called the *bone marrow*, which contains blood-forming cells. New red blood cells, white blood cells, and platelets are made in bone marrow.
- Bones also provide the body with a place to store minerals such as calcium.

Because bones are very hard and don't change shape – at least once we reach adulthood – we might not think of bones as being alive, but they are. Like all other tissues of the body, bones have many kinds of living cells. Two main types of cells in our bones help them stay strong and keep their shape.

- *Osteoblasts* help build up bones by forming the bone matrix (the connective tissue and minerals that give bone its strength).
- *Osteoclasts* break down bone matrix to prevent too much of it from building up, and they help bones keep their proper shape.

By depositing or removing minerals from the bones, osteoblasts and osteoclasts also help control the amount of these minerals in the blood.

Osteosarcoma

Osteosarcoma is the most common type of cancer that develops in bone. Like the osteoblasts in normal bone, the cells that form this cancer make bone matrix. But the bone matrix of an osteosarcoma is not as strong as that of normal bones.

Most osteosarcomas occur in children and young adults. Teens are the most commonly affected age group, but osteosarcoma can occur at any age.

In children and young adults, osteosarcoma usually develops in areas where the bone is growing quickly, such as near the ends of the long bones. Most tumors develop in the bones around the knee, either in the distal femur (the lower part of the thigh bone) or the proximal tibia (the upper part of the shinbone). The proximal humerus (the part of the upper arm bone close to the shoulder) is the next most common site. However, osteosarcoma can develop in any bone, including the bones of the pelvis (hips), shoulder, and jaw. This is especially true in older adults.

Subtypes of osteosarcoma

Several subtypes of osteosarcoma can be identified by how they look on x-rays and under the microscope. Some of these subtypes have a better prognosis (outlook) than others.

Based on how they look under the microscope, osteosarcomas can be classified as high grade, intermediate grade, or low grade. The grade of the tumor tells doctors how likely it is that the cancer will grow and spread to other parts of the body.

High-grade osteosarcomas: These are the fastest growing types of osteosarcoma. When seen under a microscope, they do not look like normal bone and have many cells in the process of dividing into new cells. Most osteosarcomas that occur in children and teens are high grade. There are many types of high-grade osteosarcomas (although the first 3 are the most common).

- Osteoblastic
- Chondroblastic
- Fibroblastic
- Mixed
- Small cell
- Telangiectatic
- High-grade surface (juxtacortical high grade)

Other high-grade osteosarcomas include:

- Pagetoid: a tumor that develops in someone with Paget disease of the bone
- Extra-skeletal: a tumor that starts in a part of the body other than a bone
- Post-radiation: a tumor that starts in a bone that had once received radiation therapy

Intermediate-grade osteosarcomas: These uncommon tumors fall in between high-grade and low-grade osteosarcomas. (They are usually treated as if they are low-grade osteosarcomas.)

- Periosteal (juxtacortical intermediate grade)

Low-grade osteosarcomas: These are the slowest growing osteosarcomas. The tumors look more like normal bone and have few dividing cells when seen under a microscope.

- Parosteal (juxtacortical low grade)
- Intramedullary or intraosseous well differentiated (low-grade central)

The grade of the tumor plays a role in determining its stage and the type of treatment used. For more on staging, see the section "How is osteosarcoma staged?"

Other types of bone tumors

Several other types of tumors can start in the bones.

Malignant (cancerous) bone tumors

Ewing tumors are the second most common bone cancer in children. They are described in our document *Ewing Family of Tumors*.

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 our document *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, prostate cancer that spreads to the bones is still prostate cancer and is treated like prostate cancer. For more information, see the document *Bone Metastasis*.

Benign (non-cancerous) bone tumors

Not all bone tumors are cancer. Benign bone tumors do not spread to other parts of the body. They are usually not life threatening and can often be cured by surgery. There are many types of benign bone tumors.

- Osteomas are benign tumors formed by bone cells.
- Chondromas are benign tumors formed by cartilage cells.
- Osteochondromas are benign tumors with both bone and cartilage cells.

Other benign bone tumors include eosinophilic granuloma of bone, non-ossifying fibroma, enchondroma, xanthoma, benign giant cell tumor of bone, and lymphangioma.

The rest of this document covers only osteosarcoma.

What are the key statistics about osteosarcoma?

Osteosarcoma is not a common cancer. Each year, about 800 new cases of osteosarcoma are diagnosed in the United States. About 400 of these are in children and teens.

Most osteosarcomas occur in children and young adults between the ages of 10 and 30. Teens are the most commonly affected age group, but osteosarcoma can occur in people of any age. About 10% of all osteosarcomas occur in people over the age of 60.

Osteosarcomas account for about 2% of childhood cancers, but they make up a much smaller percentage of adult cancers.

The prognosis (outlook) for people with osteosarcoma depends on many factors, including the location of the tumor, whether the cancer has spread (metastasized) when it's first found, and the person's age. Statistics related to survival are discussed in the section "What are the survival rates for osteosarcoma?"

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

What are the risk factors for osteosarcoma?

A risk factor is anything that affects your 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 childhood osteosarcomas. So far, lifestyle-related factors have not been linked to osteosarcomas in adults, either.

Age

The risk of osteosarcoma is highest for those between the ages of 10 and 30, especially during the teenage growth spurt. This suggests there may be a link between rapid bone growth and risk of tumor formation. The risk goes down in middle age, but rises again in older adults (usually over the age of 60). Osteosarcoma in older adults is often linked to another cause, such as a long-standing bone disease.

Height

Children with osteosarcoma are usually tall for their age. This also suggests that osteosarcoma may be related to rapid bone growth.

Gender

Osteosarcoma is more common in males than in females. Females tend to develop it at a slightly earlier age, possibly because they tend to have their growth spurts earlier.

Race/ethnicity

Osteosarcoma is slightly more common in African Americans than in whites.

Radiation to bones

People who were treated with radiation therapy for another cancer might have a higher risk of later developing osteosarcoma in the area that was treated. Being treated at a younger age and being treated with higher doses of radiation both increase the risk of developing osteosarcoma.

It is not clear if imaging tests that use radiation, such as x-rays, CT scans, and bone scans, raise the risk of developing osteosarcoma. The amount of radiation used for these tests is many times lower than that used for radiation therapy. If there is any increased risk it is likely to be very small, but doctors try to limit the use of these types of tests in children whenever possible, just in case.

Certain bone diseases

People with certain non-cancerous bone diseases have an increased risk of developing osteosarcoma.

Paget disease of the bone: In this condition, abnormal bone tissue forms in one or more bones. It mostly affects people older than 50. The affected bones are heavy and thick but are weaker than normal bones and are more likely to break. Usually this condition by itself is not life-threatening. But bone sarcomas (mostly osteosarcoma) develop in about 1% of people with Paget disease, usually when many bones are affected.

Hereditary multiple osteochondromas: Osteochondromas are benign bone tumors formed by bone and cartilage. Each osteochondroma has a very small risk of developing into a bone sarcoma (most often a chondrosarcoma, but less often it can be an osteosarcoma).

Most osteochondromas can be cured by surgery. However, some people inherit a tendency to develop many osteochondromas starting at a young age, and it may not be possible to remove them all. The more osteochondromas a person has, the greater the risk of developing a bone sarcoma.

Inherited cancer syndromes

People with certain rare, inherited cancer syndromes have an increased risk of developing osteosarcoma.

- Retinoblastoma is a rare eye cancer of children. Some children have the inherited form of retinoblastoma (**hereditary retinoblastoma**), in which all the cells of the body have a mutation (change) in the *RB1* gene. These children also have an increased risk of developing bone or soft tissue sarcomas, including osteosarcoma. If radiation therapy is used to treat the retinoblastoma, the risk of osteosarcoma in the bones around the eye is even higher.

- The **Li-Fraumeni syndrome** makes people much more likely to develop certain types of cancer, including breast cancer, brain tumors, osteosarcoma, and other types of sarcoma. This syndrome is usually caused by a mutation of the *TP53* tumor suppressor gene.

- Children with **Rothmund-Thomson syndrome** are short and tend to have skeletal problems and rashes. They also are more likely to develop osteosarcoma. This syndrome is caused by abnormal changes in the *REQL4* gene.

- Other rare inherited conditions, including **Bloom syndrome**, **Werner syndrome**, and **Diamond-Blackfan anemia**, have also been linked to an increased risk of osteosarcoma.

The way in which inherited DNA changes make some people more likely to develop osteosarcoma is explained in the section “Do we know what causes osteosarcoma?”

Do we know what causes osteosarcoma?

Researchers have found that osteosarcoma is linked with a number of other conditions, which were described in "What are the risk factors for osteosarcoma?" But the cause of most osteosarcomas is not clear at this time.

Scientists have learned how certain changes in our DNA can cause cells to become cancerous. DNA is the chemical in each of our cells that makes up our genes – the instructions for nearly everything our cells do. We usually look like our parents because they are the source of our DNA. But DNA affects more than how we look. It influences our risks for developing certain diseases, including some kinds of cancer.

Some genes (parts of our DNA) control when our cells grow, divide to make 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 DNA changes that turn on oncogenes or turn off tumor suppressor genes.

Some people inherit DNA mutations (changes) from a parent that increase their risk of cancer. In this situation, all of the cells in the body carry the same gene change. These are called *germline* or *inherited* mutations. Usually, however, cancer-causing changes are acquired during life rather than inherited before birth. In this case, the change occurs only in the cells that will develop the cancer. These are called *somatic* or *acquired* gene changes.

Inherited gene changes

Some inherited DNA mutations cause syndromes that are linked with an increased risk of osteosarcoma. For example:

The Li-Fraumeni syndrome is usually caused by inherited mutations that turn off the *TP53* tumor suppressor gene. These mutations give a person a very high risk of developing one or more types of cancer, including breast cancer, brain tumors, osteosarcoma, and other cancers.

Inherited changes in the retinoblastoma (*RB1*) tumor suppressor gene increase the risk of developing retinoblastoma, a type of eye cancer that affects children. Children with this gene change also have an increased risk for developing osteosarcoma.

If you are concerned you or your child might possibly have an inherited gene change, talk with your doctor about whether genetic testing might be helpful. You can also read more about this in our document Genetic Testing: What You Need to Know.

Acquired gene changes

Most osteosarcomas are not caused by inherited DNA mutations. They are the result of gene changes acquired during the person's lifetime. These changes are present only in the cancer cells and are not passed on to children.

Although radiation therapy is very useful in treating some forms of cancer, it can also cause cancer by damaging DNA. This is why people who get radiation therapy to treat another cancer are more likely to later develop osteosarcoma in the treated site.

Other DNA changes have no clear cause. They may result from random errors that occur when cells reproduce. Before a cell divides, it must copy its DNA so that both new cells have the same set of instructions. Sometimes mistakes are made during this copying process. Cells that are dividing quickly are more likely to create new cells with mistakes in their DNA, which increases the risk that a cancer such as osteosarcoma may develop. This may be why some normal situations (such as the teenage growth spurt) and diseases (such as Paget disease of bone) that cause rapid bone growth increase the risk of osteosarcoma.

Other than radiation, there are no known lifestyle-related or environmental causes of osteosarcoma, so it is important to remember that there is nothing people with these cancers could have done to prevent them.

Researchers now understand some of the gene changes that occur in osteosarcomas, but it's not always clear what causes these changes. As we learn more about what causes osteosarcoma, hopefully we will be able to use this knowledge to develop ways to better prevent and treat it.

Can osteosarcoma 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 osteosarcoma.

Most known risk factors for osteosarcoma (age, height, race, gender, and certain bone diseases and inherited conditions) cannot be changed. Other than radiation therapy, there are no known lifestyle-related or environmental causes of osteosarcoma, so at this time there is no way to protect against most of these cancers.

Can osteosarcoma be found early?

At this time, there are no widely recommended screening tests for this cancer. (Screening is testing for cancer in people without any symptoms.)

Still, most osteosarcomas are found at an early stage, before they have clearly spread to other parts of the body. Symptoms such as bone pain or swelling often prompt a visit to a doctor. (For more on this, see the section “Signs and symptoms of osteosarcoma”)

People with certain bone diseases or in families known to carry inherited conditions that raise the risk of this cancer (listed in “What are the risk factors for osteosarcoma?”) should talk with their doctors about the possible need for increased monitoring for this disease. This type of cancer usually does not run in families, but looking out for the early signs of cancer is important if it is to be treated successfully.

Signs and symptoms of osteosarcoma

Osteosarcomas are usually found because of the symptoms they cause.

Pain and swelling

Pain in the affected bone (usually around the knee or in the upper arm) is the most common symptom of osteosarcoma. At first, the pain might not be constant and may be worse at night. The pain often increases with activity and may result in a limp if the tumor is in a leg bone.

Swelling in the area is another common symptom, although it may not occur until several weeks after the pain starts. Depending on where the tumor is, it may be possible to feel a lump or mass.

Limb pain and/or swelling are very common in normal, active children and teens. They are much more likely to be caused by normal bumps and bruises, so they might not prompt a doctor visit right away. This can delay a diagnosis. If your child has these symptoms and they do not go away within a few weeks (or they get worse), see a doctor so that the cause can be found and treated, if needed.

These symptoms are less common in adults, so they should be a sign to see a doctor even sooner.

Bone fractures (breaks)

Although osteosarcoma might weaken the bone it develops in, the bones often do not break. Telangiectatic osteosarcomas, which are rare, tend to weaken bones more than other forms of osteosarcoma and are more likely to cause a fracture at the tumor site.

People with a fracture next to or through an osteosarcoma often describe a limb that was sore for a few months and suddenly became very painful when the fracture occurred.

How is osteosarcoma diagnosed?

Osteosarcomas are usually found when a person goes to the doctor because of signs or symptoms they are having. If a bone tumor is suspected, tests will be needed to find out for sure.

Medical history and physical exam

If a person has signs or symptoms that suggest a tumor in or around a bone, the doctor will want to take a complete medical history to find out more about the symptoms. A physical exam can provide information about a possible tumor, as well as other health problems. For example, the doctor may be able to see or feel an abnormal mass.

The doctor may also look for problems in other parts of the body. When people (especially adults) do have cancer in the bones, it's often the result of cancer that started somewhere else and then spread to the bones.

If the doctor suspects a person could have osteosarcoma (or another type of bone tumor), more tests will be done. These might include imaging tests, biopsies, and/or lab tests.

Imaging tests

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

- To help find out if a suspicious area might be cancer
- To help determine if a cancer may have started in another part of the body
- To learn how far cancer has spread
- To help determine if treatment is working
- To look for signs that the cancer may have come back

Patients who have or may have osteosarcoma will have one or more of these tests.

Bone x-ray

This is often the first test done if a doctor suspects a bone tumor. Doctors can often recognize a bone tumor such as osteosarcoma based on plain x-rays of the bone. But other imaging tests might be needed as well.

Even if results of an x-ray strongly suggest a person has osteosarcoma, a biopsy will still be needed to confirm that it is cancer rather than some other problem, such as an infection.

Magnetic resonance imaging (MRI) scan

MRI scans provide detailed images of soft tissues in the body. These scans make detailed images using radio waves and strong magnets instead of x-rays, so no radiation is involved. A contrast material called *gadolinium* may be injected into a vein before the scan to better see details.

Often, an MRI scan is done to get a more detailed look at a bone mass seen on an x-ray. MRI scans can usually show if the mass is likely to be a tumor, an infection, or some type of bone damage from other causes. MRI scans can also help show the exact extent of a tumor, as they provide a detailed view of the marrow inside bones and the soft tissues around the tumor. Sometimes, the MRI can help find small bone tumors several inches away from the main tumor (called *skip metastases*). Knowing the extent of an osteosarcoma is very important when planning surgery. An MRI scan usually gives better details than a CT scan (described below).

An MRI scan can take up to an hour. You (or your child) may have to lie on a table that slides inside a narrow tube, which is confining and can be distressing. Newer, more open MRI machines can help with these feelings, but the test still requires staying still for long periods of time. The machines also make buzzing and clicking noises that may be disturbing. Sometimes, younger children are given medicine to help keep them calm or even asleep during the test.

Computed tomography (CT) scan

The CT scan uses x-rays to make detailed cross-sectional images of parts of the body. If a bone x-ray shows a tumor, CT scans are sometimes used to see if the tumor has grown into nearby muscle, fat, or tendons, although MRI is often better for this. A CT scan of the chest is often done to look for spread of the cancer to the lungs. CT scans may also be done to look for the spread of the cancer to other parts of the body.

Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around a person lying on a table. A computer then combines these pictures into detailed images of slices of the part of the body being studied.

Before the test, you (or your child) may be asked to drink a contrast solution and/or get an intravenous (IV) injection of a contrast dye that helps better outline abnormal areas in the body. If the contrast dye is to be injected, you (or your child) may need an IV line. The contrast may cause some flushing (a feeling of warmth, especially in the face). Some people are allergic and get hives. Rarely, more serious reactions like trouble breathing or low blood pressure can occur. Be sure to tell the doctor if you (or your child) have any allergies or have ever had a reaction to any contrast material used for x-rays.

A CT scanner has been described as a large donut, with a narrow table in the middle opening. During the test, the table slides in and out of the scanner. You (or your child) will need to lie still on the table while the scan is being done. CT scans take longer than regular x-rays, and

you might feel a bit confined by the ring while the pictures are being taken. In some cases, children may need to be sedated before the test to stay still and help make sure the pictures come out well.

Chest x-ray

This test is sometimes done to see if cancer has spread to the lungs. It can find larger tumors, but it is not as good as a CT scan for spotting smaller tumors. If a CT scan of the chest is done, a chest x-ray probably won't be needed.

Bone scan

A bone scan can help show if a cancer has spread to other bones, and is often part of the workup for people with osteosarcoma. This test is useful because it can show the entire skeleton at once. (A positron emission tomography [PET] scan, described below, 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 areas of damaged bone throughout the entire skeleton over the course of a couple of hours. You (or your child) then lie on a table for about 30 minutes while a special camera detects the radioactivity and creates a picture of the skeleton. Younger children may be given medicine to help 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. Hot spots may suggest areas of cancer, but other bone diseases can also cause the same pattern. To make an accurate diagnosis, other tests such as plain x-rays, 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 *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, you (or 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 useful information about the whole body.

PET scans can help show the spread of osteosarcomas to the lungs, other bones, or other parts of the body, and can also help in following the response to treatment.

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

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

Biopsy

The results of imaging tests might strongly suggest that a person has some type of bone cancer, 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 osteosarcoma from other types of bone 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 surgical treatment should be planned together, and the same orthopedic surgeon should do both the biopsy and the surgery. Proper planning of the biopsy can help prevent later complications and might reduce the amount of surgery needed later on.

There are 2 main types of biopsies.

Needle biopsy

For these biopsies, the doctor uses a hollow needle to remove a small sample of the tumor. The biopsy is usually done with local anesthesia, where numbing medicine is injected into the skin and other tissues over the biopsy site. In some cases, sedation or general anesthesia (where the patient is asleep) may be needed.

Often, the doctor can aim the needle by feeling the suspicious area if it is near the surface of the body. If the tumor can't be felt because it is too deep, the doctor can guide the needle into the tumor while viewing a CT scan. This is called a *CT guided needle biopsy*.

Core needle biopsy: In a core needle biopsy, the doctor uses a large, hollow needle to remove a small cylinder of tissue from the tumor.

Fine needle aspiration (FNA) biopsy: For an FNA biopsy, the doctor uses a very thin needle attached to a syringe to withdraw (aspirate) a small amount of fluid and some cells from the tumor. This type of biopsy is rarely used for bone tumors.

Surgical (open) biopsy

In an open biopsy, the surgeon cuts through the skin, exposes the tumor, and then cuts out a piece of it. These biopsies are usually done with the patient under general anesthesia (in a deep sleep). They can also be done using a nerve block, which numbs a large area.

This type of biopsy must be done by an expert in bone tumors, or it could result in problems later on. For example, if the tumor is on the arm or leg, it's possible the chance for saving the limb may be lost. If possible, the incision in the skin used in the biopsy should be lengthwise along the arm or leg because this is the way the incision will be made during the operation to remove the cancer. The entire scar of the original biopsy will also have to be removed, so making the biopsy incision this way lessens the amount of tissue that needs to be removed later on.

Lab tests

Testing the biopsy samples

All samples removed by biopsy are sent to a pathologist (a doctor specializing in lab tests) to be looked at under a microscope. Tests looking for chromosome or gene changes in the tumor cells may also be done. These tests can help tell osteosarcoma from other cancers that look like it under the microscope, and they can sometimes help predict whether the osteosarcoma is likely to respond to therapy.

If osteosarcoma is diagnosed, the pathologist will assign it a grade, which is a measure of how quickly the cancer is likely to grow and spread, based on how it looks under a microscope. Cancers that look somewhat like normal bone tissue are described as low grade, while those that look very abnormal are called high grade. For more on grading, see the section "How is osteosarcoma staged?"

Blood tests

Blood tests are not needed to diagnose osteosarcoma, but they may be helpful once a diagnosis is made. For example, high levels of chemicals in the blood such as alkaline phosphatase and lactate dehydrogenase (LDH) can suggest that the osteosarcoma may be more advanced than it appears.

Other tests such as blood cell counts and blood chemistry tests are done before surgery and other treatments to get a sense of a person's overall health. These tests are also used to monitor a person's health while they are getting chemotherapy.

How is osteosarcoma staged?

The stage of a cancer is a standard summary of how far a cancer has spread. The treatment and prognosis (outlook) for osteosarcoma depend, to a large extent, on the stage of the cancer when it is first diagnosed.

The stage of an osteosarcoma is based on the results of physical exams, imaging tests, and any biopsies that have been done, which were described in the section "How is osteosarcoma diagnosed?"

A staging system is a standard way for the cancer care team to sum up the extent of the cancer. When trying to figure out the best course of treatment, doctors often use a simple system that divides osteosarcomas into 2 groups – localized and metastatic. Doctors can also use more formal staging systems, described below, to describe the extent of an osteosarcoma in more detail.

Staging can be confusing. If you have any questions about the stage of the cancer, ask your (child's) doctor to explain it to you in a way you understand.

Localized versus metastatic osteosarcoma

Localized osteosarcoma

A localized osteosarcoma is seen only in the bone it started in and possibly the tissues next to the bone, such as muscle, tendon, or fat.

About 4 out of 5 osteosarcomas are thought to be localized when they are first found. But even when imaging tests don't show that the cancer has spread to distant areas, most patients are likely to have very small areas of cancer spread that can't be detected with tests. This is why chemotherapy is an important part of treatment for most osteosarcomas. If it isn't given, the cancer is more likely to come back after surgery.

Doctors further divide localized osteosarcomas into 2 groups:

- **Resectable** cancers are those in which all of the visible tumor can be removed by surgery.
- **Non-resectable** (or **unresectable**) osteosarcomas can't be removed completely by surgery.

Metastatic osteosarcoma

A metastatic osteosarcoma has clearly spread to other parts of the body. Most often it spreads to the lungs, but it can also spread to other bones, the brain, or other organs.

About 1 out of 5 osteosarcoma patients has metastatic spread at the time of diagnosis. These patients are harder to treat, but some can be cured if the metastases can be removed by surgery. The cure rate for these patients improves markedly if chemotherapy is also given.

Musculoskeletal Tumor Society (MSTS) Staging System

One system commonly used to stage osteosarcoma is the MSTS system, also known as the *Enneking system*. It is based on 3 key pieces of information:

- The **grade** of the tumor (G)

- The extent of the main (primary) **tumor** (T)
- If the tumor has **metastasized** (spread) to nearby lymph nodes (bean-sized collections of immune system cells) or other organs (M)

The grade of a tumor is a measure of how likely it is to grow and spread, based on how it looks under the microscope. Tumors are either low grade (G1) or high grade (G2). 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.

The extent of the primary tumor is classified as either intracompartmental (T1), meaning it has basically remained within the bone, or extracompartmental (T2), meaning it has extended beyond the bone into other nearby structures.

Tumors that have not spread to the lymph nodes or other organs are considered M0, while those that have spread are M1.

These factors are combined to give an overall stage, using Roman numerals from I to III. Stages I and II are further divided into A for intracompartmental tumors or B for extracompartmental tumors.

Stage	**Grade**	**Tumor**	**Metastasis**
IA	G1	T1	M0
IB	G1	T2	M0
IIA	G2	T1	M0
IIB	G2	T2	M0
III	G1 or G2	T1 orT2	M1

In summary:

- Low-grade, localized tumors are stage I.
- High-grade, localized tumors are stage II.
- Metastatic tumors (regardless of grade) are stage III.

AJCC staging system

Another system sometimes used to stage bone cancers is the American Joint Commission on Cancer (AJCC) system. The AJCC uses one system to describe all bone cancers, including

osteosarcomas. 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 look under a microscope. Low-grade tumor cells look more like normal cells and are less likely to grow and spread quickly, while high-grade tumor cells look more abnormal.

Numbers 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 has "skipped" to another site or sites within the same bone.

N categories of bone cancer

N0: The cancer has not spread to regional (nearby) lymph nodes.

N1: The cancer has spread to nearby lymph nodes.

M categories of bone cancer

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

M1a: The cancer has spread only to the lung.

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

Grades of bone cancer

Note: The grades used for the AJCC system are different from those in the MSTS system. There are other differences between the systems as well. To avoid confusion, it may help to ask your (child's) doctor which staging system he or she uses.

GX: Grade can't be assessed

G1, G2: Low grade

G3, G4: High grade

Stage grouping

Once the T, N, and M categories and the grade of the bone cancer have been determined, the information is combined into 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 to 4), and are sometimes divided further.

Stage IA

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

Stage IB

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

Stage IIA

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

Stage IIB

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

Stage III

T3, N0, M0, G3 or G4: The tumor has "skipped" to other sites in the same bone. It is high grade. It has not spread to nearby lymph nodes or to distant parts of the body.

Stage IVA

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

Stage IVB (if either of these applies)

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

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

What are the survival rates for osteosarcoma?

Survival rates are often used by doctors as a standard way of discussing the prognosis (outlook) of a person with a certain type and stage of cancer. Some patients or parents of children with cancer may want to know the survival statistics for people 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 the survival statistics for osteosarcoma given in the next few paragraphs, skip to the next section.

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

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

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they can't predict what will happen in any particular person's case. Many other factors can affect a person's outlook, such as the subtype and location of the osteosarcoma and how well the cancer responds to treatment. Your (child's) doctor can tell you if the numbers below may apply, as he or she is familiar with the aspects of your (child's) situation.

Localized tumors

With current treatment, the 5-year survival rate for people with localized osteosarcoma is in the range of 60% to 80%. These cancers are more likely to be cured if they are resectable; that is, if all of the visible tumor can be removed (resected) by surgery. (For high-grade osteosarcomas that can be resected completely, chemotherapy is still an essential part of treatment. Without it, the cancer is still very likely to come back.)

Metastatic tumors

If the osteosarcoma has already spread when it is first found, the 5-year survival rate is about 15% to 30%. The survival rate is closer to 40% if the cancer has spread only to the lungs (as opposed to having reached other organs), or if all of the tumors (including metastases) can be removed with surgery.

Other factors that may affect prognosis

As noted above, factors other than the stage of the cancer can also affect survival rates. For example, factors that have been linked with a better prognosis include:

- Being younger (child or young adult, as opposed to older adult)
- Being female
- The tumor being on an arm or leg (as opposed to the hip bones)
- The tumor(s) being completely resectable
- Normal blood alkaline phosphatase and LDH levels
- The tumor having a good response to chemotherapy

How is osteosarcoma treated?

General treatment information

Great advances have been made in the treatment of osteosarcoma during the past few decades. In the 1960s the only treatment available was amputation, and only a small number of patients survived 2 years or more after diagnosis.

Since that time, doctors have found that chemotherapy given before and after surgery will cure many people with osteosarcoma. It can also allow some people who previously would have needed to have a limb amputated to have limb-sparing surgery instead.

Making treatment decisions

Once osteosarcoma is found and staged, the cancer care team will talk with you about treatment options. It's important to be sure you understand your options. Ask your cancer care team questions. You can find some good questions to ask in the section "What should you ask the doctor about osteosarcoma?"

Because osteosarcoma is rare, only doctors in major cancer centers have a lot of experience treating these cancers.

For children and teens, a team approach is recommended that includes the child's pediatrician as well as children's cancer specialists. Treatment is best done at a children's cancer center. For adults with osteosarcoma, 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 trained to treat cancer with chemotherapy and other drugs)
- A radiation oncologist (a doctor trained to treat cancer with radiation therapy)
- A pathologist (a doctor specializing in lab tests to diagnose and classify diseases)
- A physiatrist (a doctor specializing in rehabilitation and physical therapy)

For both adults and children, the team will also include other doctors, physician assistants, nurse practitioners, nurses, psychologists, social workers, rehabilitation specialists, and other health professionals. For more information, see our document *Children Diagnosed With Cancer: Understanding the Health Care System*.

The types of treatment used for osteosarcomas include:

- Surgery
- Chemotherapy
- Radiation therapy (in certain cases)

Most often, both chemotherapy and surgery are needed.

All of these treatments may have side effects, but many of them can be made less troublesome. Your medical team will help you take care of the side effects and can help you work closely with nutritionists, psychologists, social workers, and other professionals to understand and deal with medical problems, stress, and other issues related to the treatment.

Because many of these issues can be more complex for cancer in children and teens, many people will be involved in your child's overall care. As a parent, taking care of a child with cancer can be a very big job. It's important to remember that you will have a lot of help. It's also important for you to know that the health professionals who treat children with osteosarcoma are using the experience and knowledge gained from many decades of studying the treatment of this disease.

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.

If you would like to learn more about clinical trials that might be right for you, start by asking your 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 medical needs, or see "Clinical Trials" 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 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 your 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 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 *Complementary and Alternative Medicine* to learn more.

Help getting through cancer treatment

Your 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 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 you 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 next few sections describe the types of treatment used for osteosarcomas. This is followed by a discussion of the most common treatment approaches based on the extent of the cancer

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.

Surgery for osteosarcoma

Surgery is an important part of treatment for virtually all osteosarcomas. 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*.

A pathologist will look at the removed tissue under a microscope to see if the margins (outer edges) contain 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.

The type of surgery done depends on the location of the tumor. Although all operations to remove osteosarcomas are complex, tumors in the limbs (arms or legs) are generally not as hard to remove as those at the base of the skull, in the spine, or in the pelvis.

Tumors in the arms or legs

Tumors in the arms or legs might be treated with either:

- Limb-salvage (limb-sparing) surgery: removing the cancer and some surrounding normal tissue but leaving the limb basically intact
- Amputation: removing the cancer and all or part of an arm or leg

Limb-salvage surgery: Most patients with tumors in the arms or legs can have limb-sparing surgery, but this depends on where the tumor is, how big it is, and whether it has grown into nearby structures.

Limb-salvage 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 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 cancer has grown into these structures, they will need to be removed along with the tumor. In such cases, amputation may sometimes be the best option.

The section of bone that is removed along with the osteosarcoma is replaced with a bone graft (piece of bone from another part of the body or from another person) or with an internal

prosthesis (a man-made device used to replace part or all of a bone) made of metal and other materials.

Complications of limb-salvage surgery can include infections and grafts or rods that become loose or broken. Limb-salvage surgery patients might need more surgery in the following years, and some might still eventually need an amputation.

Using an internal prosthesis in growing children is especially challenging. In the past, it required occasional operations to replace the prosthesis with a longer one as the child grew. Newer prostheses have become very sophisticated and can often 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.

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

Amputation: For some patients, amputation may be the best option. For example, if the patient has a large tumor that extends into the nerves and/or the blood vessels, it might not be possible to save the limb.

The surgeon decides how much of the arm or leg needs to be amputated based on the results of MRI scans and an examination of removed tissue by the pathologist during the surgery. Surgery is planned so that muscles and the skin will form a cuff around the remaining bone. This cuff will fit into the end of a prosthetic (artificial) limb.

Reconstructive surgery can help some patients who lose a limb to function as well as possible. For example, if the leg must be amputated mid-thigh (including the knee joint), the lower leg and foot can be rotated and attached to the thigh bone, so that the ankle functions as a new knee joint. This surgery is called *rotationplasty*. Of course, the patient would still need a prosthetic limb to extend the leg.

With proper physical therapy, the patient is often able to walk on his/her own 3 to 6 months after leg amputation.

If the osteosarcoma is in the upper arm and amputation is needed, in some cases the part of the arm with the tumor can be removed and the lower arm reattached so that the patient has a functional, but much shorter, arm.

Rehabilitation after surgery: This may be the hardest part of all the treatments, and this discussion cannot describe it completely. Patients and parents should meet with a rehabilitation specialist before surgery to learn about their options and what might be required after surgery.

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

When only the tumor and part of the bone is removed in a limb-sparing operation, the situation can sometimes be even more complicated, especially in growing children. Further operations might be needed in the coming years to replace an internal prosthesis with one more suited to their growing body size.

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

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 support and encouragement are needed for all patients (see "What happens after treatment for osteosarcoma?").

Tumors that start in other areas

Pelvic tumors can often be hard to remove completely with surgery. But if the tumor responds well to chemotherapy first, surgery (sometimes followed by radiation therapy) may get rid of all of the cancer. 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.

For a tumor in the lower jaw bone, the entire lower half of the jaw may be removed and later replaced with bones from other parts of the body. If the surgeon can't remove all of the tumor, radiation therapy may be used as well.

For tumors in areas like the spine or the skull, it may not be possible to remove all of the tumor safely. Cancers in these bones may require a combination of treatments such as chemotherapy, surgery, and radiation.

Surgical treatment of metastases

If the osteosarcoma has spread to other parts of the body, these tumors need to be removed to have a chance at curing the cancer.

If osteosarcoma spreads, most often it is to the lungs. Surgery to remove these metastases must be planned very carefully. Before the operation, the surgeon considers the number of tumors, their location (one lung or both lungs), their size and how they responded to chemotherapy, and the general health of the patient. Since the chest CT scan done before surgery might not show all of the lung tumors, the surgeon will have a treatment plan in case more tumors are found during the operation.

Patients who have tumors in both lungs and respond well to chemotherapy can have surgery on one side of the chest at a time. Removing tumors from both lungs at the same time may be another option.

Some lung metastases may not be able to be removed because they are too big or are too close to important structures in the chest (such as large blood vessels). Patients whose general health is not good (because of poor nutritional status or heart, liver, or kidney problems) might not be able to withstand the stress of anesthesia and surgery to remove metastases.

A small number of osteosarcomas spread to other bones or to other organs like the kidneys, liver, or brain. Whether these tumors can be removed with surgery depends on their size, location, and other factors.

Side effects of surgery

Short-term risks and side effects: Surgery to remove an osteosarcoma 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 might require 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. Most osteosarcomas occur in bones of the arms or legs, and some of the long-term issues from surgery on these tumors are described above.

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 chemotherapy 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.

As mentioned above, physical therapy and rehabilitation is very important for patients who have had surgery for osteosarcoma. 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 general information on surgery as a treatment for cancer, see our document *Understanding Cancer Surgery: A Guide for Patients and Families*.

Chemotherapy for osteosarcoma

Chemotherapy (chemo) is the use of drugs to treat cancer. The drugs are usually given into a vein or artery and can reach and destroy cancer cells throughout the body.

Chemo is an important part of the treatment for most people with osteosarcoma (although some patients with low-grade osteosarcoma might not need it). Most osteosarcomas don't appear to have spread beyond the main tumor when they are first found. But in the past, when doctors tried to treat these cancers with surgery alone, they would often come back in other parts of the body, where they would be very hard to control. Giving chemo along with surgery helps lower the risk of these cancers coming back.

Most osteosarcomas are treated with chemo before surgery (known as *neoadjuvant chemotherapy*) for about 10 weeks and then again after surgery (known as *adjuvant chemotherapy*) for up to a year. People with high-grade osteosarcomas that responded well to chemo before surgery usually get the same chemo drugs after surgery. People whose tumors responded poorly usually get different chemo after surgery.

Doctors give chemo in cycles, with each period of treatment followed by a rest period to give the body time to recover. Each cycle typically lasts for a few weeks. The drugs used most often to treat osteosarcoma include:

- Methotrexate (given in high doses along with leucovorin to help prevent side effects)
- Doxorubicin (Adriamycin)
- Cisplatin or carboplatin
- Epirubicin
- Ifosfamide
- Cyclophosphamide
- Etoposide
- Gemcitabine
- Topotecan

Usually, 2 or more drugs are given together. Some common combinations of drugs include:

- High-dose methotrexate, doxorubicin, and cisplatin (sometimes with ifosfamide)
- Doxorubicin and cisplatin
- Ifosfamide and etoposide
- Ifosfamide, cisplatin (or carboplatin), and epirubicin

Many experts recommend that the drugs be given in very high doses when possible. This can affect the bone marrow (where new blood cells are made), which can result in dangerously low white blood cell levels and an increased risk of infections. In these cases, drugs called

growth factors (such as filgrastim, also known as G-CSF) may be given along with the chemo to help the body make new white blood cells as quickly as possible.

Before starting chemo, the doctor might advise putting a catheter (a thin, soft tube) into a large vein in the chest. This is sometimes called a *venous access device* (VAD) or *central venous catheter* (CVC). The catheter is inserted surgically while the patient is sedated (sleepy) or 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 health care team give chemo and other drugs and draw blood samples without having to stick needles into the veins each time. The catheter usually remains in place for several months, and can make having chemo less painful. If such a device is used, the health care team will teach you how to care for it to reduce the risk of problems such as infections.

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. Because of this, doctors can give them higher doses of chemo to try 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: Many chemo drugs can cause side effects, such as:

- Nausea and vomiting
- Loss of appetite
- Diarrhea
- Hair loss
- Mouth sores

Because chemo can damage the blood-producing cells of the bone marrow, patients may have low blood cell counts, which can result in:

- Increased chance of infection (from a shortage of white blood cells)
- Bleeding or bruising after minor cuts or injuries (from a shortage of platelets)
- Fatigue or shortness of breath (from low red blood cell counts)

Most of these side effects are short-term and tend to go away after treatment is finished. Often there are ways to lessen these side effects. For example, drugs can be given to help prevent or reduce nausea and vomiting, or to help get blood counts back to normal levels. Be sure to discuss any questions you have about side effects with the cancer care team, and tell them about any side effects so that they can be controlled.

Side effects of certain drugs: Some side effects are specific to certain drugs. Many of these side effects are rare, but they are possible. Before treatment, ask your cancer care team about the possible side effects of the drugs you or your child will be getting.

Ifosfamide and cyclophosphamide can damage the lining of the bladder, which can cause blood in the urine. The chance of this happening can be lowered by giving a drug called *mesna* during chemotherapy, along with plenty of fluids.

Cisplatin and carboplatin may cause nerve damage (called *neuropathy*) leading to numbness, tingling, or pain 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. These drugs can sometimes affect hearing, especially of high-pitched sounds. Kidney damage can also occur after treatment. Giving lots of fluid before and after the drug is infused can help prevent this.

Etoposide can also cause nerve damage. It can also increase the risk of later developing a cancer of white blood cells, known as *acute myeloid leukemia*. Fortunately, this is not common.

High-dose methotrexate can damage the white matter of the brain (called *leukoencephalopathy*) and the liver or kidneys. Before starting high-dose methotrexate, medicines are given to help protect the kidneys. Methotrexate blood levels may be checked to see how much leucovorin (also called *folinic acid*) should be given to help limit any damage to normal tissues.

Doxorubicin (Adriamycin) and epirubicin can cause heart damage over time. This risk goes up as the total amount of the drug that is given goes up, so doctors are careful to limit the total dose. Your (child's) doctor may order a heart function test before and during treatment to see if this drug is affecting the heart. A drug called *dexrazoxane* may be given along with the chemo to help lessen the possible damage.

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.

The doctors and nurses will watch closely for side effects. Don't hesitate to ask your cancer care team any questions about side effects.

For more information on the possible late or long-term side effects of chemo, including infertility and second cancers, see the section "Long-term effects of cancer treatment for osteosarcoma."

Tests to check for side effects of chemotherapy: Before each treatment, your (or your child's) doctor will check lab test results to be sure the liver, kidneys, and bone marrow are working well.

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

An audiogram might be done to check hearing, which can be affected by certain chemo drugs.

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

For more information on chemotherapy, see the "Chemotherapy" section of our website.

Radiation therapy for osteosarcoma

Radiation therapy uses high-energy rays or particles to kill cancer cells. Osteosarcoma cells are not easily killed by radiation, so radiation therapy doesn't play a major role in treating this disease.

Radiation therapy can be useful in some cases where the tumor can't be removed completely by surgery. For example, osteosarcoma can start in hip bones or in the bones of the face, particularly the jaw. In these situations, often it's not possible to remove all of the cancer. As much as possible is removed, and then radiation is given to try to kill the remaining cancer cells. Chemotherapy is then often given after the radiation.

Radiation can also be used to help slow tumor growth and control symptoms like pain and swelling if the cancer has come back or surgery is not possible.

External beam radiation therapy

This is the type of radiation therapy most often used to treat osteosarcoma. It focuses high-energy beams on the tumor from a machine outside the body to kill the cancer cells.

Before treatments start, the radiation team takes careful measurements with imaging tests such as MRI scans to determine the correct angles for aiming the radiation beams and the proper dose of radiation.

Most often, radiation treatments are given 5 days a week for several weeks. Each treatment is much like getting an x-ray, although the dose of radiation is much higher. The treatment is

not painful. For each session, you (or your child) will lie on a special table while a machine delivers the radiation from precise angles.

Each treatment lasts only a few minutes, although the setup time – getting you (or your child) into place for treatment – usually takes longer. Young children may be given medicine to make them sleep so they will not move during the treatment.

Newer radiation techniques, such as intensity modulated radiation therapy (IMRT) and conformal proton beam therapy, let doctors aim treatment at the tumor more precisely while reducing how much radiation nearby healthy tissues get. This may offer a better chance of increasing the success rate and reducing side effects. Many doctors now recommend using these approaches when they are available (see "What's new in osteosarcoma research and treatment?").

Possible side effects: The side effects of external radiation therapy depend on the dose of radiation and where it is aimed. Short-term problems can 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. Talk with your (child's) doctor about the possible side effects because there may be ways to relieve some of them.

In children, radiation therapy can affect the growth of the bones. For example, radiation to the bones in one leg might result in it being much shorter than the other. Radiation to the 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 jaw area might affect the salivary glands, which could lead to dry mouth and tooth problems.
- Radiation therapy to the spine or skull might affect the nerves in the spinal cord or brain. This could lead to nerve damage, headaches, and trouble thinking, which usually become most serious 1 or 2 years after treatment. Radiation to the spine might cause numbness or weakness in part of the body.
- 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 a child's 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.

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. The higher the dose of radiation, the more likely this is to occur, but the overall risk is small and should not keep children who need radiation from getting treatment.

To lower the risk of serious long-term effects from radiation, doctors try to use the lowest dose of radiation therapy that is still effective. 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.

Radioactive drugs (radiopharmaceuticals)

Bone-seeking radioactive drugs, such as samarium-153, are sometimes used to slow tumor growth and treat symptoms such as pain in people with advanced osteosarcoma. These drugs are injected into a vein and collect in the bones. Once there, the radiation they give off kills the cancer cells.

These drugs are especially helpful when cancer has spread to many bones, since external beam radiation would need to be aimed at each affected bone. In some cases, these drugs are used together with external beam radiation aimed at the most painful bone metastases.

The major side effect of these drugs is a lowering of blood cell counts, which could increase the risk for infections or bleeding, especially if the blood counts are already low.

For more detailed information on radiation therapy, see the "Radiation Therapy" section of our website or our document *Understanding Radiation Therapy: A Guide for Patients and Families*.

Treatment based on the extent of the osteosarcoma

Treatment for osteosarcoma depends on several factors, including the extent, location, and grade of the cancer, and on a person's age and overall health.

Localized, resectable osteosarcoma

These cancers have not been found to have spread to other parts of the body, and all of the visible tumor can be removed (resected) completely by surgery.

High grade: Most osteosarcomas are high grade, meaning they will likely grow and spread quickly if not treated. The usual sequence of treatment for these cancers is as follows:

- Biopsy to establish the diagnosis.
- Chemotherapy, usually for about 10 weeks.
- Surgery to remove the tumor, preferably by the same surgeon who did the biopsy. If cancer is found at the edge of the surgery specimen (meaning some cancer might have been left behind), a second surgery might be done to try to remove any remaining cancer. Radiation therapy might be given to the area as well.

- More chemo (for up to a year). If the initial chemo killed most of the cancer cells, the same drugs are often given again after surgery. If the initial chemo didn't work well, different drugs might be tried.

Chemotherapy is an important part of treatment for these cancers. Even when imaging tests don't show that the cancer has spread to distant areas, many patients are likely to have very small areas of cancer spread that can't be detected with tests. If chemotherapy isn't given, the cancer is more likely to come back after surgery.

In rare cases, surgery might be the first treatment (before chemo), especially for people who are elderly.

Low grade: A small number of osteosarcomas are low grade, meaning they are likely to grow slowly. Patients with low-grade, resectable osteosarcomas can often be cured with surgery alone (without chemotherapy). However, if the tumor removed by surgery is found to be high grade, chemotherapy might be recommended.

Localized, non-resectable osteosarcoma

These cancers have not been found to have spread to other parts of the body, but they can't be removed (resected) completely by surgery. For example, they may be too large or too close to vital structures in the body to be resected completely.

As with other osteosarcomas, a biopsy is needed first to establish the diagnosis.

Chemotherapy is usually the first treatment for these cancers. If the tumor shrinks enough to become resectable it will be removed with surgery. This is followed by more chemotherapy for up to a year.

If the tumor is still unresectable after chemotherapy, radiation therapy can often be used to try to keep the tumor under control and to help relieve symptoms. This may be followed by more chemotherapy.

Metastatic osteosarcoma

These cancers have already been found to have spread to distant parts of the body when they are diagnosed. Most often they have spread to the lungs. As with other osteosarcomas, a biopsy is needed first to establish the diagnosis.

Chemotherapy is usually the first treatment for these cancers. If all of the tumors are thought to be resectable after chemotherapy, they are removed with surgery, sometimes in more than one operation. This is followed by more chemo for up to a year.

If some of the tumors remain unresectable after chemo, radiation therapy can often be used to try to keep them under control and to help relieve symptoms. This may be followed by more chemo.

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

Recurrent osteosarcoma

Recurrent cancer means that the cancer has come back after treatment. It may come back locally (near where the first tumor was) or in distant organs. Most of the time, if osteosarcoma recurs it will be in the lungs.

If possible, surgery to remove the tumor(s) is the preferred treatment, as it offers the best chance for long-term survival. If the cancer recurs at the original site on an arm or leg after limb-sparing surgery, amputation of the limb may be recommended.

Chemotherapy may be used for recurrent cancers as well, although its role in these cases is not clearly defined. If the cancer is not resectable, radiation therapy may also be used to help keep its growth in check and help relieve symptoms. Because these tumors can be hard to treat, clinical trials of newer treatments may be a good option.

More treatment information for osteosarcoma

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

The COG is the world's largest organization devoted to research on cancer in children and teens. The COG website, www.childrensoncologygroup.org, provides information to help support children and their families from diagnosis, through treatment, and beyond.

What should you ask the doctor about osteosarcoma?

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 osteosarcoma do I (does my child) have? Will this affect treatment?
- Has the cancer spread beyond the bone it started in?
- What is the stage of the cancer and what does that mean?
- Do we need to do other tests before we can decide on treatment?
- How much experience do you have treating this type of cancer?

- Will 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?
- How long will treatment last? What will it be like? Where will it be done?
- How will treatment affect our daily lives?
- What should I (we) do to be ready for treatment?
- What are the possible 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?
- Are there fertility issues we need to consider?
- What are the chances of the cancer coming back with these treatment plans? 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 you can plan work or school schedules. You may also want to ask about second opinions or about available clinical trials.

What happens after treatment for osteosarcoma?

Following treatment for osteosarcoma, the main concerns for most people are the short- and long-term effects of the cancer and its treatment, and concerns about the cancer 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 you (or your child) the best chance for recovery and long-term survival.

Follow-up care

After treatment is over, it's very important to go to all follow-up appointments. During these visits, doctors will ask about symptoms, do physical exams, and may order blood tests or imaging tests such as CT scans or x-rays. Follow-up visits are needed to check for cancer recurrence or spread, as well as possible side effects of treatment. This is the time for you to ask the health care team any questions you need answered and to discuss any concerns you might have.

You or your child will probably see the oncologist and the orthopedic surgeon and get imaging tests every few months during the couple of years after treatment, and less often after that if there are no issues.

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

Some chemotherapy drugs can cause problems with hearing or heart damage. People who get these drugs may also have audiograms to check hearing or tests to check heart function.

Almost any cancer treatment can have side effects. Some may last for weeks or months, but others can last longer or might not show up until months or even years later. Tell the cancer care team about any symptoms or side effects so they can help manage them.

Keeping good medical records

As much as you may want to put the experience behind you once treatment is completed, it is also very important to keep good records of your (child's) medical care during this time. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. This can be very helpful later on if you (or your child) change doctors. Be sure the doctors have the following information, 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 (or your child) stayed in the hospital, copies of the discharge summaries that doctors prepare when patients are sent home
- If chemo 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.

Social, emotional, and other issues in people with osteosarcoma

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

Most osteosarcomas develop during the teenage or young adult years, a very sensitive time in a person's life. Osteosarcoma 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 how they do some everyday tasks, including certain school, work, or recreational activities. These effects are often greatest during the first year of treatment, but they can be long-lasting 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.

Some children and teens may have emotional or psychological issues that need to be addressed during and after treatment. Depending on their age, they may also have some problems with normal functioning and school work. These can often be overcome with support and encouragement. Doctors and other members of the health care team can also often recommend special support programs and services to help after treatment.

Cancer care teams usually recommend that school-age children and teens attend school as much as possible. This can help them maintain a sense of daily routine and keep their friends informed about what is going on.

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 situations like this. In this program, health educators visit the school and tell students about the diagnosis, treatment, and changes the person may go through. They also answer any questions from teachers and classmates. (For more information, see our document *Children Diagnosed With Cancer: Returning to School*.)

Centers that treat many patients with osteosarcoma might have programs to introduce new patients to others who have already finished treatment. This can give patients an idea of what to expect during and after treatment, which is very important. Seeing another person with osteosarcoma doing well is often helpful. There are also support groups that encourage athletics and full use of the limbs. Many amputees or people with prostheses 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 cancer 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 arise. 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 osteosarcoma, but for many people, the experience can eventually be positive, helping to establish strong self-values. Other people 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 on 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.

Late and long-term effects of treatment for osteosarcoma

More young people with osteosarcoma are now surviving this cancer. But the treatment may affect their health later in life, so watching for health effects as they get older has become more of a concern in recent years.

Just as the treatment of cancer in young people requires a very specialized approach, so does their care and follow-up after treatment. The earlier any 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 type of cancer, the specific cancer treatments they received, doses of cancer treatment, and age when receiving treatment.

For example, as described in the "Surgery for osteosarcoma" section, the after-effects of surgery 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 (due to certain chemo drugs or radiation therapy to the chest)
- Loss of hearing (due to certain chemo drugs)
- Slowed or decreased growth and development (in the bones or overall)
- Changes in sexual development and ability to have children (see below)
- Learning problems in younger children
- 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 may 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 osteosarcoma treatment, but they can occur. Older girls and 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 may remain low. Radiation to the pelvis can also damage reproductive organs, which could affect fertility.

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

Development of a second cancer

Rarely, some types of chemotherapy can cause a second type of cancer (such as leukemia), years after the osteosarcoma is cured. Radiation therapy can also raise the risk of a new cancer at the site of the treatment. But the importance of treating the osteosarcoma generally far outweighs this small risk. For more information on second cancers, see our document *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 of childhood cancer survivors throughout their lives, the Children's Oncology Group (COG) has developed long-term follow-up guidelines for survivors of childhood cancers. These guidelines can help you know what to watch for, what types of screening tests should be done to look for problems, and how late effects are 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 download them for free at the COG website: www.survivorshipguidelines.org. The guidelines are written for health care professionals. Patient versions of some of the guidelines are available (as "Health Links") on the site as well, but we urge you to discuss them with a doctor.

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

What's new in osteosarcoma research and treatment?

Research on osteosarcoma is now being done at medical centers, university hospitals, and other institutions across the world.

Understanding osteosarcoma

Researchers are learning more about what makes osteosarcoma cells different from normal bone cells. Knowing more about the changes in osteosarcoma cells might eventually result in specific treatments that exploit these changes. For example, researchers have found that osteosarcoma cells often have large amounts of a substance called GD2 on their surfaces. Drugs that target GD2 are already used to treat neuroblastoma (another cancer often seen in children), and are now being studied for use against osteosarcoma.

Tests of gene changes called *gene expression profiling* might help predict the behavior of each tumor, such as how they will respond to certain types of chemotherapy. These are still being tested in clinical trials.

Treatment

Great advances have been made in treating osteosarcoma in the past few decades. Still, more research is needed to learn how best to manage hard-to-treat osteosarcomas, such as those that have already spread when they are found. Many clinical trials are focusing on treating osteosarcoma using a variety of strategies.

Surgery

Doctors now have a much better understanding of the typical growth and spread of osteosarcomas than they did in the past. This, along with newer imaging tests that better define the extent of tumors, lets them plan surgeries to remove the cancer while sparing as much normal tissue as possible.

Some newer types of internal prostheses (man-made devices used to replace pieces of bone) can now be expanded without the need for more surgery. This is especially important for children, who in the past often needed several operations to replace the prosthesis with a larger one as they grew.

Radiation therapy

Osteosarcoma cells are not killed easily by radiation, so high doses are needed to have an effect. This has limited the use of radiation, because such high doses can often cause unacceptable side effects. Newer forms of radiation let doctors focus the radiation more precisely on the tumor. This limits the doses received by nearby healthy tissues and may allow higher doses to be used on the tumor itself.

Intensity-modulated radiation therapy (IMRT) is an example of an advanced form of therapy. In this technique, radiation beams are shaped to fit the tumor and aimed at the tumor from several angles. The intensity (strength) of the beams can also be adjusted to limit the dose reaching nearby normal tissues. This may let 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).

A newer approach is to use radioactive particles instead of x-rays to deliver the radiation. One example uses protons, which are positive parts of atoms. Unlike x-rays, which release energy both before and after they hit their target, protons cause little damage to tissues they pass through and then release their energy after traveling a certain distance. Doctors can use this property to deliver more radiation to the tumor and to do less damage to nearby normal tissues. As with IMRT, proton beam therapy 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 in the United States at this time.

An even newer approach uses carbon ions, which are heavier than protons and cause more damage to cancer cells. This therapy is still in the earliest stages of development and is only available in a few centers around the world.

Doctors are also studying newer forms of radioactive drugs to treat osteosarcoma that has spread to many bones. One example is radium-223 (Xofigo), which might work better than the drugs now used.

Chemotherapy

Clinical trials are being done to determine the best combinations of chemotherapy (chemo) drugs, as well as the best time to give them. Newer chemo drugs are being studied as well.

The lungs are the most common place for osteosarcoma to spread. Inhaled forms of some chemo drugs (such as cisplatin) are being studied for patients whose cancer has spread to their lungs. Early results have been promising.

Other new forms of treatment

Chemo drugs are often effective against osteosarcoma, but sometimes they don't work or the cancer becomes resistant to them over time. Researchers are studying newer types of drugs that attack osteosarcoma cells in different ways

Immunotherapy drugs: Clinical trials are looking into ways to help the patient's own immune system recognize and attack the osteosarcoma cells. An experimental immune-modulating drug called *muramyl tripeptide* (also known as MTP or mifamurtide) has been shown to help some patients when added to chemotherapy.

Targeted therapy drugs: Doctors are also studying new medicines that target specific molecules on the cancer cells. These are known as *targeted therapies*. Some of these are man-made versions of immune system proteins, known as *monoclonal antibodies*. These antibodies attach to certain proteins on the cancer cell and help to stop the growth or kill the cancer cells. Examples now being studied include antibodies against the insulin-like growth factor receptor 1 (IGF-1R), a protein that may help cancer cells grow.

Other targeted drugs being studied for use against osteosarcoma include:

- Drugs that affect a tumor's ability to make new blood vessels, such as sorafenib (Nexavar) and pazopanib (Votrient).
- Drugs that target the mTOR protein, such as temsirolimus (Torisel) and everolimus (Afinitor).

Drugs that affect the bones: Other drugs that target bone cells called *osteoclasts* may also be useful against osteosarcoma. Bisphosphonates are a group of drugs that are already used to treat osteoporosis (bone thinning) and certain cancers that have spread to the bone. Some of these drugs, such as pamidronate and zoledronic acid, are now being studied for use in osteosarcoma as well. Another drug that affects bones, known as *saracatinib* (AZD0530), is also being studied.

Additional resources for osteosarcoma

More information from your American Cancer Society

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:

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 (COG)
Website: www.childrensoncologygroup.org

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

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

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

National Cancer Institute
Toll-free number: 1-800-422-6237 (1-800-4-CANCER)
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: 1-800-532-6459 (1-800-5-FAMILY)
Website: www.children-cancer.org

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

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

Provides information about disabilities and disability-related issues for families, educators, and other professionals.

Websites for teens and children

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

Website has animated stories and interactive programs to teach kids about chemo and procedures that are done in the hospital; also has videos specifically for teens and 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! powered by Alex's Lemonade Stand
Toll-free number: 1-866-333-1213
Website: www.supersibs.org

> Supports, honors, and recognizes brothers and sisters of children diagnosed with cancer so they may face the future with strength, courage, and hope. Alex's Lemonade Stand is restarting SuperSibs in 2014 so there may be some delays with resuming support services.

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

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

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