BONE CANCER

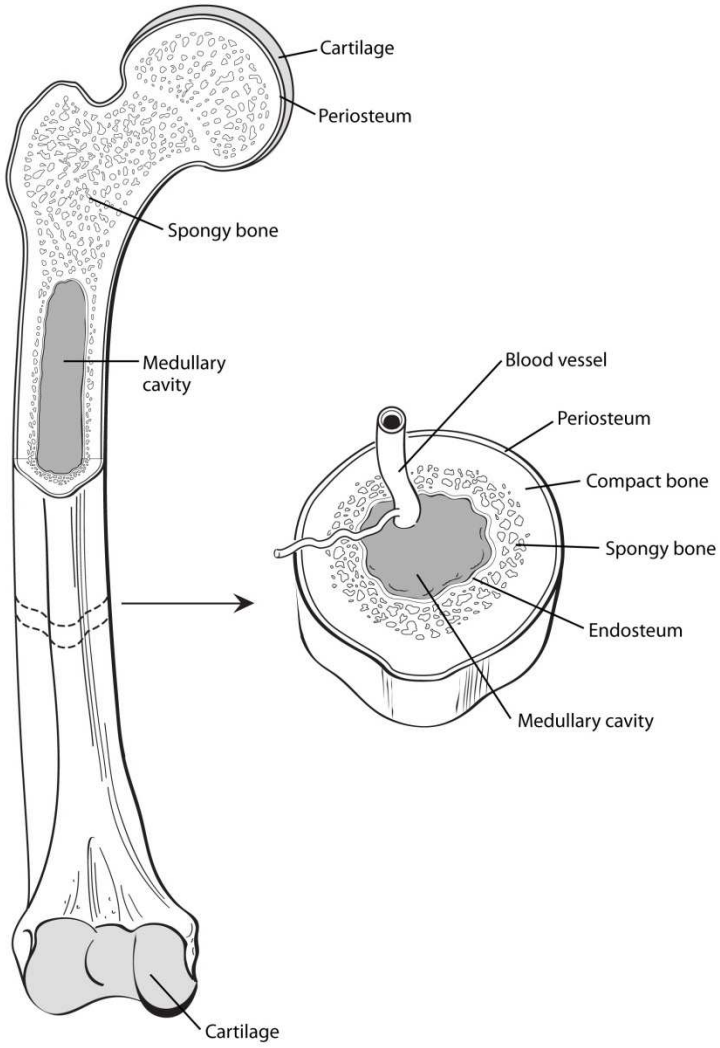
What is bone cancer?

Bone cancer starts in the bone. 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?*

Normal bone tissue

To understand bone cancer, it helps to understand a little about normal bone tissue.

Bone is the supporting framework of your body. Most bones are hollow. The outer part of bones is a network of fibrous tissue called *matrix* onto which calcium salts are laid down.



The hard outer layer of bones is made of compact (cortical) bone, which covers the lighter spongy (trabecular) bone inside. The outside of the bone is covered with a layer of fibrous tissue called *periosteum*. Some bones are hollow and have a space called the *medullary cavity* which contains the soft tissue called *bone marrow* (discussed below). The tissue lining the medullary cavity is called *endosteum*. At each end of the bone is a zone of a softer form of bone-like tissue called *cartilage*.

Cartilage is softer than bone but more firm than most tissues. It is made of a fibrous tissue matrix mixed with a gel-like substance that does not contain much calcium.

Most bones start out as cartilage. The body then lays calcium down onto the cartilage to form bone. After the bone is formed, some cartilage may remain at the ends to act as a cushion between bones. This cartilage, along with ligaments and some other tissues connect bones to form a joint. In adults, cartilage is mainly found at the end of some bones as part of a joint. It

is also seen at the place in the chest where the ribs meet the sternum (breastbone) and in parts of the face. The trachea (windpipe), larynx (voice box), and the outer part of the ear are other structures that contain cartilage.

Bone itself is very hard and strong. Some bone is able to support as much as 12,000 pounds per square inch. It takes as much as 1,200 to 1,800 pounds of pressure to break the femur (thigh bone). The bone itself contains 2 kinds of cells. The *osteoblast* is the cell that lays down new bone, and the *osteoclast* is the cell that dissolves old bone. Bone often looks as if it doesn't change much, but the truth is that it is very active. Throughout our bodies, new bone is always forming while old bone is dissolving.

In some bones the marrow is only fatty tissue. The marrow in other bones is a mixture of fat cells and blood-forming cells. The blood-forming cells produce red blood cells, white blood cells, and blood platelets. Other cells in the marrow include plasma cells, fibroblasts, and reticuloendothelial cells.

Cells from any of these tissues can develop into a cancer.

Types of bone tumors

Most of the time when someone with cancer is told they have cancer in the bones, the doctor is talking about a cancer that has spread to the bones from somewhere else. This is called *metastatic cancer.* It can be seen in many different types of advanced cancer, like breast cancer, prostate cancer, and lung cancer. When these cancers in the bone are looked at under a microscope, they look like the tissue they came from. For example, if someone has lung cancer that has spread to bone, the cells of the cancer in the bone still look and act like lung cancer cells. They do not look or act like bone cancer cells, even though they are in the bones. Since these cancer cells still act like lung cancer cells, they still need to be treated with drugs that are used for lung cancer.

For more information about metastatic bone cancer, please see our document called *Bone Metastasis,* as well as the document on the specific place the cancer started (*Breast Cancer, Lung Cancer, Prostate Cancer,* etc.).

Other kinds of cancers that are sometimes called "bone cancers" start in the blood forming cells of the bone marrow − not in the bone itself. The most common cancer that starts in the bone marrow and causes bone tumors is called *multiple myeloma.* Another cancer that starts in the bone marrow is *leukemia,* but it is generally considered a blood cancer rather than a bone cancer. Sometimes lymphomas, which more often start in lymph nodes, can start in bone marrow. Multiple myeloma, lymphoma, and leukemia are not discussed in this document. For more information on these cancers, refer to the individual document for each.

A *primary* bone tumor starts in the bone itself. True (or primary) bone cancers are called *sarcomas*. Sarcomas are cancers that start in bone, muscle, fibrous tissue, blood vessels, fat tissue, as well as some other tissues. They can develop anywhere in the body.

There are several different types of bone tumors. Their names are based on the area of bone or surrounding tissue that is affected and the kind of cells forming the tumor. Some primary bone tumors are *benign* (not cancerous), and others are *malignant* (cancerous). Most bone cancers are sarcomas.

Benign bone tumors

Benign tumors do not spread to other tissues and organs and so are not usually life threatening. They are generally cured by surgery. Types of benign bone tumors include:

- Osteoid osteoma (OS-tee-oyd OS-tee-oh-ma)
- Osteoblastoma (OS-tee-oh-blas-**TOE**-muh)
- Osteochondroma (OS-tee-oh-kon-DROH-muh)
- Enchondroma (en-kon-DROH-muh)
- Chondromyxoid (kon-dro-MIX-oyd) fibroma.

These benign tumors are not discussed further in this document, which is limited to bone cancers.

Malignant bone tumors

Osteosarcoma: Osteosarcoma (also called *osteogenic sarcoma*) is the most common primary bone cancer. This cancer starts in the bone cells. It most often occurs in young people between the ages of 10 and 30, but about 10% of osteosarcoma cases develop in people in their 60s and 70s. It is rare in middle-aged people, and is more common in males than females. These tumors develop most often in bones of the arms, legs, or pelvis. This cancer is not discussed in detail in this document, but is covered in our document called *Osteosarcoma.*

Chondrosarcoma: Chondrosarcoma (KON-droh-sar-KOH-muh) is a cancer of cartilage cells. It is the second most common primary bone cancer. This cancer is rare in people younger than 20. After age 20, the risk of getting a chondrosarcoma goes up until about age 75. Women get this cancer as often as men.

Chondrosarcomas can develop anywhere there is cartilage. Most develop in bones such as the pelvis, leg bone or arm bone. Occasionally, chondrosarcoma will develop in the trachea, larynx, and chest wall. Other sites are the scapula (shoulder blade), ribs, or skull.

Benign (non-cancerous) tumors of cartilage are more common than malignant ones. These are called *enchondromas*. Another type of benign tumor that has cartilage is a bony projection capped by cartilage called an *osteochondroma*. These benign tumors rarely turn into cancer. There is a slightly higher chance of cancer developing in people who have many of these tumors, but this is still not common.

Chondrosarcomas are classified by grade, which measures how fast they grow. The grade is assigned by the pathologist (a doctor specially trained to examine and diagnose tissue samples under a microscope). The lower the grade, the slower the cancer grows. When a cancer is slow growing, the chance that it will spread is lower and so the outlook is better. Most chondrosarcomas are either low grade (grade I) or intermediate grade (grade II). High-grade (grade III) chondrosarcomas, which are the most likely to spread, are less common.

Some chondrosarcomas have distinctive features under a microscope. These variants of chondrosarcoma can have a different prognosis (outlook) than usual chondrosarcomas.

- *Dedifferentiated* (DEE- dih-feh-REN-shee-AY-ted) *chondrosarcomas* start out as typical chondrosarcomas but then some parts of the tumor change into cells like those of a high-grade sarcoma (such as high grade forms of malignant fibrous histiocytoma [HIS-tee-oh-sy-TOH-muh], osteosarcoma, or fibrosarcoma). This variant of chondrosarcoma tends to occur in older patients and is more aggressive than usual chondrosarcomas.

- *Clear cell chondrosarcomas* are rare and grow slowly. They rarely spread to other parts of the body unless they have already come back several times in the original location.

- *Mesenchymal* (meh-ZEN-kih-mul) *chondrosarcomas* can grow rapidly, but like Ewing tumor, are sensitive to treatment with radiation and chemotherapy.

Ewing tumor: Ewing tumor is the third most common primary bone cancer, and the second most common in children, adolescents, and young adults. This cancer (also called *Ewing sarcoma*) is named after the doctor who first described it in 1921, Dr. James Ewing. Most Ewing tumors develop in bones, but they can start in other tissues and organs. The most common sites for this cancer are the pelvis, the chest wall (such as the ribs or shoulder blades), and the long bones of the legs or arms. This cancer is most common in children and teenagers and is rare in adults older than 30. Ewing tumors occur most often in white people and are very rare among African Americans and Asian Americans. More detailed information about this cancer can be found in our document called *Ewing Family of Tumors.*

Malignant fibrous histiocytoma: Malignant fibrous histiocytoma (MFH) more often starts in soft tissue (connective tissues such as ligaments, tendons, fat, and muscle) than in bones. This cancer is also known as *pleomorphic undifferentiated sarcoma*, especially when it starts in soft tissues. When MFH occurs in bones, it usually affects the legs (often around the knees) or arms. This cancer most often occurs in elderly and middle-aged adults and is rare among children. MFH mostly tends to grow locally, but it can spread to distant sites, like the lungs.

Fibrosarcoma: This is another type of cancer that develops more often in soft tissues than it does in bones. Fibrosarcoma usually occurs in elderly and middle-aged adults. Bones in the legs, arms, and jaw are most often affected.

Giant cell tumor of bone: This type of primary bone tumor has benign and malignant forms. The benign (non-cancerous) form is most common. Giant cell bone tumors typically affect

the leg (usually near the knees) or arm bones of young and middle-aged adults. They don't often spread to distant sites, but tend to come back where they started after surgery (this is called *local recurrence*). This can happen several times. With each recurrence, the tumor becomes more likely to spread to other parts of the body. Rarely, a malignant giant cell bone tumor spreads to other parts of the body without first recurring locally.

Chordoma: This primary tumor of bone usually occurs in the base of the skull and bones of the spine. It develops most often in adults older than 30, and is about twice as common in men as in women. Chordomas tend to grow slowly and often do not spread to other parts of the body, but they often come back in the same area if they are not removed completely. The lymph nodes, the lungs, and the liver are the most common areas for secondary tumor spread.

Other cancers that develop in bones

Non-Hodgkin lymphomas

Non-Hodgkin lymphoma generally develops in lymph nodes but sometimes starts in the bone. Primary non-Hodgkin lymphoma of the bone is often a widespread disease because multiple sites in the body are usually involved. The outlook is similar to other non-Hodgkin lymphomas of the same subtype and stage. Primary lymphoma of the bone is given the same treatment as lymphomas that start in lymph nodes − it is not treated like a primary bone sarcoma. For more information see our document *Non-Hodgkin Lymphoma.*

Multiple myelomas

Multiple myeloma almost always develops in bones, but doctors do not consider it a primary bone cancer because it develops from the plasma cells of the bone marrow (the soft inner part of some bones). Although it causes bone destruction, it is no more a bone cancer than is leukemia. It is treated as a widespread disease. At times, myeloma can be first found as a single tumor (called a *plasmacytoma*) in a single bone, but most of the time it will spread to the marrow of other bones. For more information see our document *Multiple Myeloma.*

What are the key statistics about bone cancer?

The American Cancer Society's estimates for cancer of the bones and joints for 2016 are:

- About 3,300 new cases will be diagnosed
- About 1,490 deaths from these cancers are expected.

Primary cancers of bones account for less than 0.2% of all cancers.

In adults, over 40% of primary bone cancers are chondrosarcomas. This is followed by osteosarcomas (28%), chordomas (10%), Ewing tumors (8%), and malignant fibrous

histiocytoma/fibrosarcomas (4%). The remainder of cases are several rare types of bone cancers.

In children and teenagers (those younger than 20 years), osteosarcoma (56%) and Ewing tumors (34%) are much more common than chondrosarcoma (6%).

Chondrosarcomas develop most often in adults, with an average age at diagnosis of 51. Less than 5% of cases occur in patients younger than 20.

Chordomas are also more common in adults. Less than 5% of cases occur in patients younger than 20.

Both osteosarcomas and Ewing tumors occur most often in children and teens.

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

What are the risk factors for bone cancer?

A *risk factor* is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancers of the lung, mouth, larynx, bladder, kidney, and several other organs. But having a risk factor, or even several, does not mean that you will get the disease. Most people with bone cancers do not have any apparent risk factors.

Genetic disorders

A very small number of bone cancers (especially osteosarcomas) appear to be hereditary and are caused by defects (mutations) in certain genes.

Osteosarcomas

Children with certain rare inherited syndromes have an increased risk of developing osteosarcoma.

- The **Li-Fraumeni (**lee-FRAH-meh-nee) **syndrome** makes people much more likely to develop several types of cancer, including breast cancer, brain cancer, osteosarcoma, and other types of sarcoma. Most of those cases are caused by a mutation of the *p53* tumor suppressor gene, but some are caused by mutations in the gene *CHEK2*.
- Another syndrome that includes bone cancer is the **Rothmund-Thomson syndrome**. Children with this syndrome are short, have skeletal problems, and rashes. They also are more likely to develop osteosarcoma. This syndrome is caused by abnormal changes in the gene *REQL4*.

- **Retinoblastoma** is a rare eye cancer of children that can be hereditary. The inherited form of retinoblastoma is caused by a mutation (abnormal copy) of the *RB1* gene. Those with this mutation also have an increased risk of developing bone or soft tissue sarcomas. Also, if radiation therapy is used to treat the retinoblastoma, the risk of osteosarcoma in the bones around the eye is even higher.

Finally, there are families with several members who have developed osteosarcoma without inherited changes in any of the known genes. The gene defects that may cause cancers in these families haven't been discovered yet.

Chondrosarcomas

Multiple exostoses (sometimes called *multiple osteochondromas*) syndrome is an inherited condition that causes many bumps on a person's bones. These bumps are made mostly of cartilage. They can be painful and deform and/or fracture bones. This disorder is caused by a mutation in any one of the 3 genes *EXT1*, *EXT2*, or *EXT3*. Patients with this condition have an increased risk of chondrosarcoma.

An enchondroma is a benign cartilage tumor that grows into the bone. People who get many of these tumors have a condition called *multiple enchondromatosis*. They have an increased risk of developing chondrosarcomas.

Chordomas

Chordomas seem to run in some families. The genes responsible have not yet been found, but familial chordoma has been linked to changes on chromosome 7.

Patients with the inherited syndrome *tuberous sclerosis*, which can be caused by defects (mutations) in either of the genes *TSC1* and *TSC2*, seem to have a high risk of chordomas during childhood.

Paget disease

Paget (PA-jet) disease is a benign (non-cancerous) but pre-cancerous condition that affects one or more bones. It results in formation of abnormal bone tissue and is mostly a disease of people older than 50. Affected bones are heavy, thick, and brittle. They are weaker than normal bones and more likely to fracture (break). Most of the time Paget disease is not life threatening. Bone cancer (usually osteosarcoma) develops in about 1% of those with Paget disease, usually when many bones are affected.

Radiation

Bones that have been exposed to ionizing radiation may also have a higher risk of developing bone cancer. A typical x-ray of a bone is not dangerous, but exposure to large doses of

radiation does pose a risk. For example, radiation therapy to treat cancer can cause a new cancer to develop in one of the bones in the treatment area. Being treated when you are younger and/or being treated with higher doses of radiation (usually over 60 Gy) increases the risk of developing bone cancer.

Exposure to radioactive materials such as radium and strontium can also cause bone cancer because these minerals build up in bones.

Non-ionizing radiation, like microwaves, electromagnetic fields from power lines, cellular phones, and household appliances, does not increase bone cancer risk.

Bone marrow transplantation

Osteosarcoma has been reported in a few patients who have undergone bone marrow (stem cell) transplantation.

Injuries

People have wondered whether injury to a bone can cause cancer, but this has never been proven. Many people with bone cancer remember having hurt that part of their bone. Most doctors believe that this did not cause the cancer, but rather that the cancer caused them to remember the incident or that the injury drew their attention to that bone and caused them to notice a problem that had already been present for some time.

Do we know what causes bone cancer?

The exact cause of most bone cancers is not known. However, scientists have found that bone cancers are associated with a number of other conditions, which are described in the section on risk factors. Still, most people with bone cancers do not have any known risk factors. Research is underway to learn more about the causes of these cancers.

Scientists have made great progress in understanding how certain changes in a person's DNA can cause normal cells to become cancerous. DNA carries the instructions for nearly everything our cells do. We usually look like our parents because they are the source of our DNA. However, DNA affects more than our outward appearance. It may influence our risks for developing certain diseases, including some kinds of cancer.

DNA is divided into units called *genes*. Genes carry the recipes for making proteins, the molecules that determine all cell functions. Some genes contain instructions to control when our cells grow and divide. Genes that promote cell division 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 mutations (defects) that activate oncogenes or inactivate tumor suppressor genes. Some people with cancer have DNA mutations that they inherited from a parent. These mutations increase their risk for the disease.

The DNA mutations that cause some inherited forms of bone cancers are known (see the section, “What are the risk factors for bone cancer?”). In many cases, genetic testing can be used to see if someone has one of these mutations.

Most bone cancers are not caused by inherited DNA mutations. They are the result of mutations acquired during the person’s lifetime. These mutations may result from exposure to radiation or cancer-causing chemicals, but most often they occur for no apparent reason. These mutations are present only in the cancer cells and so cannot be passed on to the patient’s children.

Scientists are making progress in understanding this process, but there are still some points that are not completely understood. As their knowledge increases, they hope to develop ways to better prevent and treat bone cancers.

Can bone cancer be prevented?

Changes in lifestyle can help prevent many types of cancer. At present, however, no known lifestyle changes can prevent bone cancers.

Can bone cancer be found early?

Tests are routinely used to detect early stages of some types of cancer (such as breast, cervical, colorectal, and skin cancer) before they cause symptoms. At this time, no special tests are routinely recommended to detect bone cancers early. The best strategy for early diagnosis is prompt attention to the signs and symptoms of this disease.

Signs and symptoms of bone cancer

Pain

Pain in the affected bone is the most common complaint of patients with bone cancer. At first, the pain is not constant. It may be worse at night or when the bone is used (for example, leg pain when walking). As the cancer grows, the pain will be there all the time. The pain increases with activity and the person might limp if a leg is involved.

Swelling

Swelling in the area of the pain may not occur until weeks later. It might be possible to feel a lump or mass depending on the location of the tumor.

Cancers in the bones of the neck can cause a lump in the back of the throat that can lead to trouble swallowing or make it hard to breathe.

Fractures

Bone cancer can weaken the bone it develops in, but most of the time the bones do not fracture (break). People with a fracture next to or through a bone cancer usually describe sudden severe pain in a limb that had been sore for a few months.

Other symptoms

Cancer in the bones of the spine can press on nerves, leading to numbness and tingling or even weakness.

Cancer can cause weight loss and fatigue. If the cancer spreads to internal organs it may cause other symptoms, too. For example, if the cancer spreads to the lung, you may have trouble breathing.

Any of these symptoms are more often due to conditions other than cancer, such as injuries or arthritis. Still, if these problems go on for a long time without a known reason, you should see your doctor.

How is bone cancer diagnosed?

A patient's symptoms, physical exam, and results of imaging tests, and blood tests may suggest that bone cancer is present. But in most cases, doctors must confirm this suspicion by examining a tissue or cell sample under a microscope (a procedure known as a *biopsy*).

Other diseases, such as bone infections, can cause symptoms and imaging results that could be confused with bone cancer. Accurate diagnosis of a bone tumor often depends on combining information about its location (what bone is affected and even which part of the bone is involved), appearance on x-rays, and appearance under a microscope.

Since a single bone metastasis can have the same signs and symptoms as a primary bone tumor, many doctors require a biopsy to diagnose a patient's first bone metastasis. After that, additional bone metastases can usually be diagnosed based on x-rays and other imaging tests.

Imaging tests to detect bone cancer

X-rays

Most bone cancers show up on x-rays of the bone. The bone at the site of the cancer may appear "ragged" instead of solid. The cancer can also appear as a hole in the bone. Sometimes doctors can see a tumor around the defect in the bone that might extend into nearby tissues (such as muscle or fat). The radiologist (doctor who specializes in reading x-rays) can often tell if a tumor is malignant by the way it appears on the x-ray, but only a biopsy can absolutely determine that.

A chest x-ray is often done to see if bone cancer has spread to the lungs.

Computed tomography (CT) scans

The CT scan is an x-ray procedure that produces detailed, cross-sectional images of your body. Instead of taking one picture, like a conventional x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image of a slice of your body. The machine creates multiple images of the part of your body that is being studied.

A CT scanner has been described as a large donut, with a narrow table in the middle opening. You 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.

CT scans are helpful in staging cancer. They help tell if your bone cancer has spread into your lungs, liver, or other organs. These scans also show the lymph nodes and distant organs where metastatic cancer might be present.

Before the test you may be asked to drink 1 or 2 pints of a contrast agent. This helps outline the stomach and intestine to make it easier to see tumors. You might also receive an IV (intravenous) line through which a different kind of contrast dye is injected. This helps better outline structures in your body.

The injection can cause some flushing (redness and warm feeling that may last hours to days). A few people are allergic to the dye and get hives. Rarely, more serious reactions like trouble breathing and low blood pressure can occur. You can be given medicine to prevent and treat allergic reactions. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays or if you have an allergy to shellfish.

CT scans can also be used to precisely guide a biopsy needle into a suspected metastasis. For this procedure, called a CT-guided needle biopsy, the patient remains on the CT scanning table while a radiologist advances a biopsy needle toward the location of the mass. CT scans are repeated until the doctors are confident that the needle is within the mass. (See the section, “Needle biopsy.”)

Magnetic resonance imaging (MRI) scans

MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into a very detailed image of parts of the body. Sometimes a contrast material called *gadolinium* is injected into your veins to better see the tumor.

MRI scans are often the best test for outlining a bone tumor. They are also particularly helpful for looking at the brain and spinal cord. MRI scans are a little more uncomfortable

than CT scans. First, they take longer -- often up to an hour. Also, you have to be placed inside a tube, which is confining and can upset people with claustrophobia (fear of enclosed spaces). The machine also makes a thumping noise that you may find disturbing. Some places provide headphones with music to block this out.

Radionuclide bone scans

This procedure helps show if a cancer has spread to other bones. It can find metastases earlier than regular x-rays. Bone scans also can show how much damage the primary cancer has caused in the bone.

For this test, the patient receives an injection of radioactive material called *technetium diphosphonate* (tek-NEE-shee-um die-**fos**-fuh-nate). The amount of radioactivity used is very low and causes no long-term effects. This substance is attracted to diseased bone cells throughout the entire skeleton. Areas of diseased bone will be seen on the bone scan image as dense, gray to black areas, called “hot spots.” These areas suggest metastatic cancer is present, but arthritis, infection, or other bone diseases can also cause a similar pattern. To distinguish among these conditions, the cancer care team may use other imaging tests or take bone biopsies.

Positron emission tomography (PET or PET) scans

PET scans use glucose (a form of sugar) that contains a radioactive atom. A special camera can detect the radioactivity. Cancer cells absorb a lot of the radioactive sugar because of their high rate of metabolism. PET scans are useful in looking for cancer throughout your entire body. It can sometimes help tell if a tumor is cancerous or benign. It is being combined with CT scans to better pinpoint some kinds of cancer.

Biopsy

A *biopsy* is a sample of tissue taken from a tumor so that it can be looked at under a microscope. This is the only way to know that the tumor is cancer and not some other bone disease. If cancer is present, the biopsy can tell the doctor if it is a primary bone cancer or cancer that started somewhere else and spread to the bone (metastasis). Several types of tissue and cell samples are used to diagnose bone cancer. It is very important a surgeon with experience in diagnosing and treating bone tumors do the biopsy procedure.

The surgeon will choose a biopsy method based on whether the tumor looks benign or malignant and exactly what type of tumor is most likely (based on the bone x-rays, the patient’s age, and the location of the tumor). Some kinds of bone tumors can be recognized from needle biopsy samples, but larger samples (from a surgical biopsy) are often needed to diagnose other types. Whether the surgeon plans to remove the entire tumor at the time of the biopsy will also influence the choice of biopsy type. The wrong kind of biopsy can sometimes make it hard later for the surgeon to remove all of the cancer without having to

also remove all or part of the arm or leg containing the tumor. It also may cause the cancer to spread.

Needle biopsy

There are 2 types of needle biopsies: *fine needle biopsies* and *core needle biopsies.* For both types, a local anesthetic is first used to numb the area for the biopsy. For fine needle aspiration (FNA), the doctor uses a very thin needle attached to a syringe to withdraw a small amount of fluid and some cells from the tumor mass. Sometimes, the doctor can aim the needle by feeling the suspicious tumor or area that is near the surface of the body. If the tumor cannot be felt because it is too deep, the doctor can guide the needle while viewing a CT scan. This is called a *CT guided needle biopsy* and it is often done by an x-ray specialist known as an *interventional radiologist.* In a core needle biopsy, the doctor uses a larger needle to remove a small cylinder of tissue (about 1/16 inch in diameter and 1/2 inch long). Many experts feel that a core needle biopsy is better than FNA to diagnose a primary bone cancer.

Surgical bone biopsy

In this procedure, a surgeon needs to cut through the skin to reach the tumor in order to remove a small piece of tissue. This is also called an *incisional biopsy*. If the entire tumor is removed (not just a small piece), it is called an *excisional biopsy*. These biopsies are often done with the patient under general anesthesia (asleep). They can also be done using a nerve block, which numbs a large area. If this type of biopsy is needed, it is important that the surgeon who will later remove the cancer also be the one to do the biopsy.

How is bone cancer staged?

Staging is a process that tells the doctor how widespread a cancer may be. It will show whether the cancer has spread and how far. The treatment and prognosis (outlook) for bone cancers depend, to a large extent, on the cancer's stage when the patient is first diagnosed.

AJCC Staging System

The American Joint Commission on Cancer (AJCC) system is used to stage all bone cancers. It combines 4 factors to determine stage that go by the initials T, N, M, and G. **T** stands for features of **t**umor (its size and if it is in more than one spot on the bone), **N** stands for spread to lymph **n**odes, **M** is for **m**etastasis (spread) to distant organs, and **G** is for the tumor's **g**rade. The grade of a tumor is based on how abnormal the cells look when seen under a microscope. The higher the number, the more abnormal the cells appeared. Higher grade cancers tend to grow and spread more quickly than lower grade tumors.

This information about the tumor, lymph nodes, metastasis, and grade is combined in a process called *stage grouping*. The stage is then described in Roman numerals from I to IV (1-4).

T stages of bone cancer

TX: Primary tumor can't be measured

T0: No evidence of the tumor

T1: Tumor is 8 cm (around 3 inches) or less

T2: Tumor is larger than 8 cm

T3: Tumor is in more than one place on the same bone

N stages of bone cancer

N0: The cancer has not spread to the lymph nodes near the tumor

N1: The cancer has spread to nearby lymph nodes

M stages of bone cancer

M0: The cancer has not spread anywhere outside of the bone or nearby lymph nodes

M1: Distant metastasis (the cancer has spread)

- **M1a:** The cancer has spread only to the lung
- **M1b:** The cancer has spread to other sites (like the brain, the liver, etc.)

Grades of bone cancer

G1-G2: Low grade

G3-G4: High grade

TNM stage grouping

After the T, N, and M stages and the grade of the bone cancer have been determined, the information is combined and expressed as an overall stage. The process of assigning a stage number is called *stage grouping*. To determine the grouped stage of a cancer using the AJCC system, find the stage number below that contains the T, N, and M stages, and the proper grade.

Stage I: All stage I tumors are low grade and have not yet spread outside of the bone.

- **Stage IA:** T1, N0, M0, G1-G2: The tumor is 8 cm or less.
- **Stage IB:** T2 or T3, N0, M0, G1-G2: The tumor is either larger than 8 cm or it is in more than one place on the same bone.

Stage II: Stage II tumors have not spread outside the bone (like stage I) but are high grade.

- **Stage IIA:** T1, N0, M0, G3-G4: The tumor is 8 cm or less.
- **Stage IIB:** T2, N0, M0, G3-G4: The tumor is larger than 8 cm.

Stage III: T3, N0, M0, G3-G4: Stage III tumors have not spread outside the bone but are in more than one place on the same bone. They are high grade.

Stage IV: Stage IV tumors have spread outside of the bone they started in. They can be any grade.

- **Stage IVA:** Any T, N0, M1a, G1-G4: The tumor has spread to the lung.
- **Stage IVB:** Any T, N1, any M, G1-G4 OR Any T, any N, M1b, G1-G4: The tumor has spread to nearby lymph nodes or to distant sites other than the lung (or both).

Even though the AJCC staging system is widely accepted and used for most cancers, bone cancer specialists tend to simplify the stages into localized and metastatic. Localized includes stages I, II, and III, while metastatic is the same as stage IV.

Survival statistics for bone cancer

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some patients 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 bone cancer 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).

Five-year *relative* survival rates assume that some people will die of other causes and compare the observed survival with that expected for people without the cancer. This is a better way to see the impact of the cancer on survival.

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

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular person's case. Many factors may affect a person's outlook, such as the type and grade of the cancer, the patient's age, where the cancer is located, the size of the tumor, and the treatment received. Your doctor can tell you how the numbers below may apply to you, as he or she is familiar with the aspects of your particular situation.

For all cases of bone cancer combined (in both adults and children), the 5-year relative survival is about 70%. For adults, the most common bone cancer is chondrosarcoma, which has a 5-year relative survival of about 80%. (Survival statistics for Ewing tumors and osteosarcoma can be found in our documents about those cancers.)

How is bone cancer treated?

General treatment information

Depending on the type and stage of your cancer, you may need more than one type of treatment. Doctors on your cancer treatment team may include:

- An orthopedic surgeon: a doctor who uses surgery to treat bone and joint problems
- An orthopedic oncologist: an orthopedic surgeon that specializes in treating cancer of the bones and joints
- A radiation oncologist: a doctor who uses radiation to treat cancer
- A medical oncologist: a doctor who uses chemotherapy and other medicines to treat cancer

Many other specialists may be involved in your care as well, including nurse practitioners, nurses, psychologists, social workers, rehabilitation specialists, and other health professionals.

The main types of treatment for bone cancer are:

- Surgery
- Radiation
- Chemotherapy
- Targeted therapy

Often, more than one type of treatment is used. For information about some of the most common approaches used based on the extent of the disease, see the section "Treating specific bone cancers."

It is important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. It's also very important to ask questions if there is anything you're not sure about. You can find some good questions to ask in the section, "What should you ask your doctor about bone cancer?"

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 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 bone cancer

Surgery is the primary (main) treatment for most bone cancers. Surgery may also be needed to obtain a biopsy of the cancer. The biopsy and the surgical treatment are separate operations, but it is very important that the doctor plans both together. Ideally, the same surgeon should do both the biopsy and the main surgery. A biopsy taken from the wrong place can lead to problems when the surgeon does the operation to remove the cancer. Sometimes a poorly placed biopsy can even make it impossible to remove the cancer without cutting off the limb.

The main goal of surgery is to remove all of the cancer. If even a few cancer cells are left behind, they can grow and multiply to make a new tumor. To try to be sure that this doesn't happen, surgeons remove the tumor plus some of the normal-appearing tissue that surrounds it. This is known as *wide-excision*. Removing some normal-looking tissue helps ensure that all of the cancer is removed. After surgery, a pathologist will look at the tissue that was removed under the microscope to see if the margins (outer edges) have cancer cells. If cancer cells were 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 is seen at the edges of the tissue, the margins are said to be *negative*, *clean*, or *clear*. A wide-excision with clean margins minimizes the risk that the cancer will grow back where it started.

Tumors in the arms or legs

Sometimes the entire limb needs to be removed in order to do a good wide-excision (and remove all of the cancer). This operation is known as an *amputation*. But most of the time the surgeon can remove the cancer without amputation. This is called *limb-salvage* or *limb-sparing surgery*. In going over treatment options, it is important to realize that there are advantages and disadvantages with either type of surgery. For example, although for many people limb-salvage seems more acceptable than amputation, it is more complex and so can have more complications. Both operations have the same overall survival rates when done by expert surgeons. Studies looking at quality of life have shown little difference in how people react to the final result of the different procedures. Perhaps the biggest concern was seen in teenagers who worry about the social effects of their operation. Emotional issues can be very important and support and encouragement are needed for all patients.

No matter which type of surgery is done, rehabilitation will be needed afterward. This can be the hardest part of treatment. If possible, the patient should meet with a specialist in rehabilitation before surgery to understand what will be involved.

Amputation: Amputation is surgery to remove part or all of a limb (an arm or leg). When used to treat cancer, amputation removes the limb part with the tumor, some healthy tissue above it, and everything below it. In the past, amputation was the main way to treat bone cancers found in the arms or legs. Now, this operation is only chosen if there is a reason not to do limb-salvage surgery. For example, an amputation may be needed if removing all of the cancer requires removing essential nerves, arteries, or muscles that would leave the limb without good function.

MRI scans and examination of the tissue by the pathologist at the time of surgery can help the surgeon decide how much of the arm or leg needs to be removed. Surgery is planned so that muscles and the skin will form a cuff around the amputated bone. This cuff fits into the end of an artificial limb (or prosthesis). After surgery, a person must learn how to use the prosthesis in rehabilitation. With proper physical therapy they are often walking again 3 to 6 months after leg amputation.

Limb-salvage surgery: The goal of limb-salvage surgery is to remove all of the cancer and still leave a working leg (or arm). Over 90% of patients with bone cancer in a limb are able to have their limb spared. This type of surgery is very complex and requires surgeons with special skills and experience. The challenge for the surgeon is to remove the entire tumor while still saving the nearby tendons, nerves, and vessels. This is not always possible. If a cancer has grown into these structures, they will need to be removed along with the tumor. This can sometimes result in a limb that is painful or can't be used. In that case, amputation may be the best option.

In this type of surgery, a wide-excision is done to remove the tumor. A bone graft or an *endoprosthesis* (**en**-doe-pros-**THEE**-sis, meaning internal prosthesis) is used to replace the bone that is lost. Endoprostheses are made of metal and other materials and can be very sophisticated. Because they may be used in growing children, some can be made longer without any extra surgery as the child grows.

Further surgery could be needed if the bone graft or endoprosthesis becomes infected, loose, or broken. Limb-salvage surgery patients may need more surgery during the following 5 years, and some may eventually need an amputation.

Rehab is much more intense after limb-salvage surgery than it is after amputation. It takes an average time of a year for patients to learn to walk again after limb-salvage of a leg. If the patient does not take part in the rehabilitation program, the salvaged arm or leg may become useless.

Reconstructive surgery: If the leg must be amputated mid-thigh, the lower leg and foot can be rotated and attached to the thigh bone. The old ankle joint becomes the new knee joint. This surgery is called *rotationplasty* (roh-TAY-shun-PLAS-tee). A prosthesis is used to make the new leg the same length as the other (healthy) leg.

If the bone tumor is located in the upper arm, the tumor may be removed and then the lower arm attached again. This leaves the patient with an arm that works but is much shorter.

Tumors in other areas

Bone cancer in the pelvis is treated with a wide-excision when possible. If needed, bone grafts can be used to rebuild the pelvic bones.

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.

For tumors in areas like the spine or the skull, it may not be possible to safely do a wide-excision. Cancers in these bones may require a combination of treatments such as curettage, cryosurgery, and radiation.

Curettage (kur-uh-**TAHZH):** In this procedure, the doctor scoops out the tumor from the bone without removing a section of the bone. This leaves a hole in the bone. In some cases, after most of the tumor has been removed, the surgeon will treat the nearby bone tissue to kill any remaining tumor cells. This can be done with cryosurgery or by using bone cement.

Cryosurgery: For this treatment, liquid nitrogen is poured into the hole that is left in the bone after the tumor was removed. This extremely cold material kills tumor cells by freezing them. This treatment is also called *cryotherapy*. After cryosurgery, the hole in the bone can be filled by bone grafts or by bone cement.

Bone cement: The bone cement PMMA (polymethylmethyacrylate) starts out as a liquid and hardens over time. It can be put into a hole in the bone in liquid form. As PMMA hardens, it gives off a lot of heat. The heat helps kill any remaining tumor cells. This allows PMMA to be used without cryosurgery for some types of bone tumors.

Surgical treatment of metastasis

To be able to cure a bone cancer, it and any existing metastases must be removed completely with surgery. The lungs are the most common site of distant spread for bone cancer. Surgery to remove bone cancer metastases to the lungs must be planned very carefully. Before the operation, the surgeon will consider the number of tumors, their location (one lung or both lungs), their size, and the person’s general condition.

The chest CT scan may not show all the tumors that truly exist. The surgeon will have a treatment plan in case more tumors are found during the operation than can be seen in the chest CT scan.

Removing all the lung metastases is probably the only chance for a cure. However, not all lung metastases can be removed. Some tumors are too big or are too close to important structures in the chest (such as large blood vessels) to be removed safely. People whose general condition is not good (due to poor nutritional status or problems with the heart, liver, or kidneys) may not be able to withstand the stress of anesthesia and surgery to remove metastases.

For more information about surgery, see our document *Understanding Cancer Surgery: A Guide for Patients and Families*.

Radiation therapy for bone cancer

Radiation therapy uses high-energy rays or particles to kill cancer cells. *External beam radiation therapy* uses radiation delivered from outside the body that is focused on the cancer. This is the type of radiation therapy that has been tried as a treatment for bone cancer.

Most bone cancers are not easily killed by radiation, and high doses are needed. These high doses can damage healthy structures like nerves in the nearby area. This is why radiation therapy is not used as a major treatment for most types of bone tumors, (except for Ewing tumors, and these are discussed in a separate document). Often radiation is used to treat bone cancers that are *unresectable* (they cannot be completely removed by surgery). Radiation may also be used after surgery if cancer cells were present in the edges of the removed tissue. Another term for this is *positive margins* (this was discussed in the section about surgery). In this case, radiation may be given to kill any cancer that may have been left behind. If the cancer comes back after treatment, radiation can help control symptoms like pain and swelling.

Intensity-modulated radiation therapy

Intensity-modulated radiation therapy (IMRT) is an advanced form of external beam radiation therapy. With this technique, a computer matches the radiation beams to the shape of the tumor and can adjust the intensity (strength) of the beams. The radiation is delivered to the tumor from several directions to reduce the amount of radiation that goes through any one area of normal tissue. Altogether, this makes it possible to reduce radiation damage to normal tissues while increasing the radiation dose to the cancer.

Proton-beam radiation

Proton-beam radiation is a special form of radiation that uses protons instead of regular x-rays to kill cancer cells. Protons are positively charged particles that are found inside all atoms. They cause little damage to the tissues they pass through but are very good at killing cells at the end of their path. This allows a high dose of radiation to be given to the tumor without hurting the normal tissue around it. Proton-beam radiation therapy requires highly specialized equipment and is not available in all medical centers. This form of radiation is very helpful in treating skull base chondrosarcomas and chordomas.

Side effects

Side effects of radiation therapy depend on what area of the body is being treated and how much radiation is used. Common side effects include:

- Fatigue (tiredness)
- Loss of appetite
- Skin changes in the area being treated, ranging from redness and hair loss to blistering and peeling
- Low blood counts
- Nausea, vomiting, and diarrhea (these are more common if radiation is given to the belly)

More information on radiation therapy can be found in the Radiation section of our website, or in our document *Understanding Radiation Therapy: A Guide for Patients and Families*.

Chemotherapy for bone cancer

Chemotherapy (chemo) is the use of drugs to treat cancer. Chemo is *systemic* therapy. This means that the drug enters the bloodstream and circulates to reach and destroy cancer cells throughout the body.

Chemo is often a part of treatment for Ewing sarcoma and osteosarcoma, but it isn't often used for other bone cancers, like chordomas and chondrosarcomas, because they aren't very sensitive to chemo and so it often doesn't work well. It can be useful for some special types of chondrosarcoma, like *dedifferentiated* and *mesenchymal*.

Chemo is sometimes used for bone cancer that has spread through the bloodstream to the lungs and/or other organs. The drugs mainly used to treat bone cancer include:

- Doxorubicin (Adriamycin®)
- Cisplatin
- Carboplatin
- Etoposide (VP-16)
- Ifosfamide (Ifex®)
- Cyclophosphamide (Cytoxan®)
- Methotrexate
- Vincristine (Oncovin®)

Usually, several drugs (2 or 3) are given together. For example, a very common combination is cisplatin and doxorubicin. Other combinations are ifosfamide and etoposide or ifosfamide and doxorubicin

Side effects of chemotherapy

Chemo kills cancer cells, but it will also damage some normal cells. Careful attention is given to avoid or minimize side effects. The side effects of chemo depend on the type of drugs, the amount taken, and the length of time they are taken.

Some common temporary side effects can include:

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

It is important to tell your cancer care team about any side effects you have so that they can be prevented or controlled.

Chemotherapy can damage the blood-producing cells of the bone marrow and lymph nodes, so patients may have low blood cell counts. Low blood cell counts can result in:

- Increased chance of infection (too few white blood cells)
- Bleeding or bruising after minor cuts or injuries (too few platelets)
- Fatigue or shortness of breath (too few red blood cells)

Some side effects are specific to particular drugs. It's important to note that many of the serious side effects are rare, but possible. Discuss these with your cancer care team if you have concerns before treatment.

Ifosfamide and cyclophosphamide can damage the lining of the bladder and cause bloody urine. This is called *hemorrhagic cystitis.* This problem can be prevented by giving a drug called *mesna* along with the chemo.

Cisplatin may cause nerve damage (called *neuropathy*) leading to problems with numbness, tingling, and even pain in the hands and feet. Kidney damage (called *nephropathy*) can also occur after treatment with cisplatin. Giving lots of fluid before and after the drug is infused can help prevent this side effect. Cisplatin can sometimes cause problems with hearing (known as *ototoxicity*). Most often patients with this problem notice problems hearing high-pitched sounds.

Over time, doxorubicin can damage the heart. The risk of this goes up as the total amount of the drug given goes up. Before giving doxorubicin, your doctor may test your heart function to make sure that it is safe to give you this drug.

The doctors and nurses will watch closely for side effects. There are treatments for most side effects, but preventing significant side effects is more important. Most, if not all, of these

side effects will eventually stop after the treatment is over. Do not hesitate to ask your cancer care team any questions about side effects.

While you are being treated, your doctor will order lab tests to be sure your liver, kidney, and bone marrow (which produces the cells in the blood) are functioning well.

- The **complete blood count (CBC)** includes levels of white blood cells, red blood cells, and platelets.
- **Chemistry panels** measure certain blood chemicals that tell doctors how well the liver and the kidneys are working. Some drugs used in chemotherapy can damage the kidneys and liver.

If a drug can damage hearing, the doctor may order a hearing test (called an *audiogram*) before giving it.

For more information about chemotherapy in general, see our document *A Guide to Chemotherapy*.

Targeted therapy for bone cancer

As researchers have learned more about the molecular and genetic changes in cells that cause cancer, they have been able to develop newer drugs that specifically target some of these changes. These drugs, often called *targeted therapy drugs*, work differently from standard chemotherapy (chemo) drugs and have different side effects. Targeted drugs are especially important in diseases such as chordomas and other bone cancers, where chemo has not been very useful.

Imatinib

Some chordomas have gene defects (mutations) that make proteins that signal the cells to grow. These genes are called *c-kit, PDGFRA*, and *PDGFRB*. The drug imatinib (Gleevec®) is a targeted therapy drug that can block the signals from these genes. This can make some tumors stop growing or even shrink a little. Imatinib is used to treat chordomas that have spread or have come back after treatment. Imatinib has been used to treat chordomas for several years, but it isn't approved by the Food and Drug Administration to treat this type of cancer. It is approved to treat more common cancers.

This drug is given as a pill, taken with food once a day. Common side effects are mild and can include diarrhea, nausea, muscle pain, and fatigue. These are generally mild. Some people taking the drug have itchy skin rashes. Fluid buildup around the eyes, feet, or abdomen can also be a problem.

Denosumab

Denosumab (Xgeva®) is a monoclonal antibody (a man-made version of an immune system protein) that binds to a protein called RANK ligand. RANK ligand normally tells cells called *osteoclasts* to break down bone, but when denosumab binds to it, that action is blocked. In patients with giant cell tumors of bone that have either come back after surgery or cannot be removed with surgery, denosumab can help shrink tumors for a while.

To treat giant cell tumors, this drug is injected under the skin (sub-q or SQ), weekly for 4 weeks, and then every 4 weeks. Often, it can take months to see tumor shrinkage.

Most side effects are mild and can include body aches, headache, and nausea. A rare but very distressing side effect of denosumab is damage to the jawbone called *osteonecrosis of the jaw* (ONJ). ONJ often appears as an open sore in the jaw that won't heal. It can lead to loss of teeth or infections of the jaw bone. Doctors don't know why this happens, but it can be triggered by having a tooth removed while taking the drug. The best treatment is also unclear, other than to stop denosumab. Maintaining good oral hygiene by flossing, brushing, making sure that dentures fit properly, and having regular dental check-ups may help prevent this. Most doctors recommend that patients have a dental checkup and have any tooth or jaw problems treated before they start taking this drug.

For more general information about drugs that are considered targeted therapy, see our document *Targeted Therapy*.

Treating specific bone cancers

For specific information on treating Ewing sarcoma and osteosarcoma, please see the American Cancer Society documents on those cancers.

Chondrosarcomas

After a biopsy confirms the diagnosis, surgery is done to remove the tumor. Again, it is important that the biopsy be done by the same surgeon who will remove the tumor. For a low-grade chondrosarcoma in an arm or leg, curettage with cryotherapy is an option. If the tumor is high-grade, limb-sparing surgery will be done if possible. Sometimes amputation is needed to completely remove the cancer. If the chondrosarcoma has spread to the lung and there are only a few metastases, they may be removed surgically.

Chondrosarcomas in the skull are hard to treat. Complete surgical removal is difficult, and may cause serious side effects. Some low-grade tumors are treated with curettage and cryosurgery.

Sometimes the patient is treated with radiation therapy. Since chondrosarcomas are resistant to radiation, high doses are required. Proton-beam radiation works well for these tumors.

Chemotherapy (chemo) is not often used to treat chondrosarcoma, because most types of chondrosarcoma are resistant to chemo. Chemo can be used to treat some special types of chondrosarcoma. For example, dedifferentiated chondrosarcoma may be treated like osteosarcoma, with chemo followed by surgery and then more chemo. Patients with mesenchymal chondrosarcomas also get chemo before surgery. These tumors are treated the same as Ewing tumors or soft tissue sarcomas.

Malignant fibrous histiocytomas (MFH)

MFH is treated the same way osteosarcoma is treated. (Please see our document, *Osteosarcoma* for more detailed information.) Often the patient is first treated with chemotherapy to shrink the tumor. Then the tumor and some surrounding normal tissue is removed (wide-excision). After resection, the bone may be reconstructed with a bone graft or a prosthesis (metallic rod). Amputation is rarely needed. In some cases, chemotherapy is also given after surgery.

Fibrosarcomas

Surgery is the main treatment for this kind of cancer, with the goal of removing the tumor and a margin of surrounding normal bone. Radiation is sometimes given after surgery if the doctor suspects that some cancer has been left behind. Radiation therapy is sometimes used instead of surgery if the tumor cannot be removed completely. Radiation is also used if a fibrosarcoma returns after surgery.

Giant cell tumors of bone

These are treated mainly with surgery. Different surgeries are used, depending on the size and location of the tumor. One option is wide-excision. This often means removing the part of the bone containing the tumor, and replacing it with a bone graft or prosthesis (such as a metal rod). If this operation can be done without seriously affecting the movement of the limb or without causing serious damage to nearby tissues, this approach provides a good likelihood of success.

Another option is curettage followed by cryosurgery. The defect (hole) in the bone can then be filled in with bone cement or a bone graft.

Radiation therapy may sometimes be used for giant cell tumors in bones where surgery may be difficult to perform without damaging nearby sensitive tissues − such as the skull and the spine. Radiation is not often used to treat giant cell tumors because if the tumor is not killed completely it may increase the chance that it comes back in the malignant form.

Amputation is rarely needed to treat a giant cell tumor.

If a giant cell bone tumor spreads to other organs, the lungs are most commonly affected. If there are only a few metastatic tumors in the lungs, it may be possible to remove them

surgically. Metastases that can't be removed can be treated with radiation or with the drug denosumab (Xgeva).

Chordomas

This primary tumor of bone most often occurs in the base of the skull or the bones of the spine. The best treatment is a wide excision to remove the tumor completely with some nearby normal tissue. This is not always possible because the spinal cord and nerves nearby may be involved. Still, as much of the tumor as possible will be removed.

Radiation is often given after surgery to lower the chance that the tumor will grow back. Proton-beam radiation, either alone or with intensity-modulated radiation therapy, is often used.

Imatinib (Gleevec) is often used for a chordoma that has spread widely. It may rarely shrink the tumors, but often can stop them from growing for a while. Studies are looking at adding other drugs to imatinib when it stops working (this is discussed in the section, "What's new in bone cancer research and treatment?"). Chemo may be tried as well, but so far it hasn't worked well by itself. Chordomas can come back, even 10 or more years after treatment, so long-term follow-up is important.

What should you ask your doctor about bone cancer?

As you cope with cancer and cancer treatment, you need to have honest, open discussions with your doctor. You should be able to ask any question no matter how small it might seem. Nurses, social workers, and other members of the treatment team may also be able to answer many of your questions.

- What kind of bone cancer do I have?
- Has my cancer spread beyond the primary site?
- What is the stage of my cancer and what does that mean?
- What treatment choices do I have?
- What do you recommend and why?
- What risks or side effects are there to the treatments you suggest?
- What are the chances of my cancer coming back with these treatment plans?
- What should I do to be ready for treatment?
- Based on what you've learned about my cancer, how long do you think I'll survive?

In addition to these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so that you can plan your work schedule. Or you might want to ask about second opinions or about clinical trials. You can find more information about communicating with your health care team in our document *Talking With Your Doctor*.

What happens after treatment for bone cancer?

For some people with bone cancer, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about cancer coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are leading full lives. Our document, *Living with Uncertainty: The Fear of Cancer Recurrence,* gives more detailed information on this.

For other people, the cancer may never go away completely. These people may get regular treatments with chemotherapy, radiation, or other therapies to try to help keep the cancer in check. Learning to live with cancer that does not go away can be difficult and very stressful. It has its own type of uncertainty. Our document, *When Cancer Doesn't Go Away*, talks more about this.

Follow-up care

When treatment ends, your doctors will still want to watch you closely. It is very important to go to all of your follow-up appointments. During these visits, your doctors will ask questions about any problems you might be having and could use exams, lab tests, or x-rays and scans to look for signs of cancer or treatment side effects. Almost any cancer treatment can have side effects. Some may last for a few weeks to months, but others can last the rest of your life. Now is the time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have.

Following extensive bone surgery, a program of rehabilitation and physical therapy will be an important part of helping you regain as much of your mobility and independence as possible.

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

Should your cancer come back, our document, *When Your Cancer Comes Back: Cancer Recurrence* can give you information on how to manage and cope with this phase of your treatment.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you might find yourself seeing a new doctor who does not know anything about your medical history. It is important for you to be able to give your new doctor the details of your diagnosis and treatment. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. Make sure you have the following information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- If you had surgery, a copy of your operative report(s)
- If you had radiation, a copy of the treatment summary
- If you were in the hospital, a copy of the discharge summary that doctors prepare when patients are sent home
- If you had chemotherapy (or targeted therapy), a list of your drugs, drug doses, and when you took them
- A copy of your x-rays and other imaging studies (these can be put on a CD or DVD)

The doctor may want copies of this information for his records, but always keep copies for yourself.

Can I get another cancer after having bone cancer?

Cancer survivors can be affected by a number of health problems, but often their greatest concern is facing cancer again. If a cancer comes back after treatment it is called a “recurrence.” But some cancer survivors may develop a new, unrelated cancer later. This is called a “second cancer.” No matter what type of cancer you have had, it is still possible to get another (new) cancer, even after surviving the first.

Unfortunately, being treated for cancer doesn’t mean you can’t get another cancer. People who have had cancer can still get the same types of cancers that other people get. In fact, certain types of cancer and cancer treatments can be linked to a higher risk of certain second cancers.

Survivors of bone and joint cancers can get any type of second cancer, but they have an increased risk of getting another bone or joint cancer (this is different than the first cancer coming back). Sometimes this is the same kind of cancer as the original tumor, but it can be a different type. For example, someone who had a chondrosarcoma can get an osteosarcoma.

Sarcoma of the soft tissues is also seen more often than expected after a cancer or the bone or joints.

Survivors of bone and joint cancer also have an increased risk of:

- Lung cancer
- Esophagus cancer
- Stomach cancer
- Colorectal cancer
- Liver cancer
- Pancreas cancer
- Acute myeloid leukemia (AML)

The risk of leukemia is linked to treatment with chemotherapy.

Follow-up after treatment

After completing treatment for bone cancer, you should see your doctor regularly. You may also have tests to look for signs that your cancer has come back or spread. Experts do not recommend any additional testing to look for second cancers in patients without symptoms. Let your doctor know about any new symptoms or problems, because they could be caused by the cancer coming back or by a new disease or second cancer.

Survivors of bone cancer should follow the American Cancer Society guidelines for the early detection of cancer.

The Children's Oncology Group has guidelines for the follow-up of patients treated for cancer as a child, teen, or young adult, including screening for second cancers. These can be found at www.survivorshipguidelines.org.

All patients should stay away from tobacco products. Smoking increases the risk of many cancers and might further increase the risk of some of the second cancers seen after bone cancer.

To help maintain good health, survivors should also:

- Achieve and maintain a healthy weight
- Adopt a physically active lifestyle
- Consume a healthy diet, with an emphasis on plant foods
- Limit consumption of alcohol to no more than 1 drink per day for women or 2 per day for men

These steps may also lower the risk of some cancers.

See *Second Cancers in Adults* for more information about causes of second cancers.

Lifestyle changes after treatment for bone cancer

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life – making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Making healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on the alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society for information and support at 1-800-227-2345. A tobacco cessation and coaching service can help increase your chances of quitting for good.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is put healthy eating habits into place. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits. You can get more information in our document *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Questions*.

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a “bone-weary” exhaustion that often doesn’t get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. Someone who has never exercised will not be able to take on the same amount of exercise as someone who plays tennis twice a week. If you haven’t been active in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you’re not doing it alone. Having family or friends involved when starting a new activity program can give you that extra boost of support to keep you going when the push just isn’t there.

If you are very tired, you will need to balance activity with rest. It is OK to rest when you need to. Sometimes it’s really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more information on dealing with fatigue, please see *Fatigue in People With Cancer* and *Anemia in People With Cancer*.

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

And long term, we know that getting regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

How does having bone cancer affect your emotional health?

When treatment ends, you may find yourself overcome with many different emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through each day. Now it may feel like a lot of other issues are catching up with you.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationship with those around you. Unexpected issues may also cause concern. For instance, as you feel better and have fewer doctor visits, you will see your health care team less often and have more time on your hands. These changes can make some people anxious.

Almost everyone who has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you do not include them. Let them in, and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You can also read our document *Distress in People with Cancer* or see the Emotional Side Effects section of our website for more information.

If treatment for bone cancer stops working

If cancer keeps growing or comes back after one kind of treatment, it is possible that another treatment plan might still cure the cancer, or at least shrink it enough to help you live longer and feel better. But when a person has tried many different treatments and the cancer has not gotten any better, the cancer tends to become resistant to all treatment. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer − when you have been through many medical treatments and nothing's working anymore. Your doctor may offer you new options, but at some point you may need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. In many cases, your doctor can estimate how likely it is the cancer will respond to the treatment you are considering. For instance, the doctor may say that more chemo or radiation might have about a 1% chance of working. Some people are still tempted to try this. But it is important to think about and understand your reasons for choosing this plan.

No matter what you decide to do, you need to feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose - the main purpose of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve bone pain caused by cancer that has spread to the bones. Or chemo might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer.

You can learn more about the changes that occur when treatment meant to cure the cancer stops working, and about planning ahead for yourself and your family, in our documents *Nearing the End of Life* and *Advance Directives* You can read them online or call us at 1-800-227-2345 to have free copies mailed to you.

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn’t mean you can’t have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more in our document *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends − times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you’ve always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

What's new in bone cancer research and treatment?

Research on bone cancer is now being done at many medical centers, university hospitals, and other institutions across the nation. There are several ongoing clinical trials focusing on bone cancer.

Chemotherapy

Some clinical trials are looking into ways to combine surgery, radiation therapy, and chemotherapy (chemo), and drugs known as targeted therapy. One study found that the combination of the chemo drug cyclophosphamide (Cytoxan) and the targeted drug sirolimus can help stop chondrosarcomas from growing for a time.

Some are testing new chemo drugs.

Targeted therapy

Targeted therapy drugs work differently from standard chemo. These drugs target certain genes and proteins in cancer cells.

One example of targeted therapy is the drug imatinib (Gleevec), which targets certain proteins made by the cancer cells in chordomas. Adding another drug to imatinib, such as the targeted therapy drug sirolimus (Rapamune®) or the chemo drug cisplatin helps stop the growth of chordomas when imatinib stops working. Another drug, panobinostat, is being studied in combination with imatanib to treat chordoma.

Lapatinib (Tykerb®) is another targeted drug that may be useful in treating chordoma. In one study of patients with tumors that had too many copies of the *EGFR* gene and/or too much EGFR protein, it helped shrink tumors and stop them from growing for a time.

Some chordomas show strong expression of parts of an insulin-like growth factor pathway. This has led to studying antibodies against the insulin-like growth factor receptor 1 (IGF-1R) in chordoma patients.

Studies of other targeted drugs are going on right now, such as nilotinib (Tasigna) and dasatinib (Sprycel) in chordoma, and pazopanib (Votrient®), everolimus (Afinitor®), and vismodegib (GDC-0449) in chondrosarcoma.

Radiation

The most common type of radiation used to treat cancer uses beams of x-rays. Proton beam radiation uses particles made up of protons (protons are small positively charged particles that are part of atoms). Another much less common form of particle radiation that can be

used to treat chordomas and chondrosarcomas is carbon ion radiation. This can be helpful in treating tumors of the skull base, but is only available in a few centers worldwide.

Genetics

In addition to clinical trials, researchers are making progress in learning about the causes of bone tumors. For example, changes to a certain part of chromosome 6 have been found in chordomas. Changes the *COL2A1* gene, which codes for a major form of collagen found in cartilage, have been found in many chondrosarcomas. Hopefully more information about the DNA changes that cause bone cancers will eventually lead to treatments aimed at these gene defects.

Additional resources for bone cancer

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:

National Cancer Institute (NCI)
Toll-free number: 1-800-422-6237 (1-800-4-CANCER)
TTY: 1-800-332-8615
Website: www.cancer.gov

> Their "Cancer Information Service" offers a wide variety of free, accurate, up-to-date information about cancer to patients, their families, and the general public; also can help people find clinical trials in their area

CancerCare
Toll-free number: 1-800-813-HOPE (1-800-813-4673)
Website: www.cancercare.org

> Provides free professional support services to anyone affected by cancer: people with cancer and their loved ones, caregivers, and the bereaved through phone counseling and online support groups; also offers a wide variety of cancer information as well as specialized programs and workshops

**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.

References: Bone cancer detailed guide

American Cancer Society. *Cancer Facts and Figures, 2016*. Atlanta, Ga: American Cancer Society; 2016.

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

Bjornsson J, McLeod RA, Unni KK, et al. Primary chondrosarcoma of long bones and limb girdles. *Cancer*. 1998;83:1945-2008.

Bovee JV, Cleton-Jansen A, Taminiau AH, Hogendoom PCW. Emerging pathways in the development of chondrosarcoma of bone and implications for targeted treatment. *Lancet Oncology*. 2005;6:599-607.

Casali PG, Stacchiotti S, Grosso F, et al. Adding cisplatin (CDDP) to imatinib (IM) reestablishes tumor response following secondary resistance to IM in advanced chordoma. 2007 ASCO Annual Meeting Proceedings Part 1. *J Clin Oncol*. 2007;25 (18S): Abstract #10038.

Casali PG, Messina A, Stacchiotti S, et al. Imatinib mesylate in chordoma. *Cancer*. 2004;101(9):2086-2097.

Chawla S, Henshaw R, Seeger L, et al. Safety and efficacy of denosumab for adults and skeletally mature adolescents with giant cell tumour of bone: interim analysis of an open-label, parallel-group, phase 2 study. *Lancet Oncol*. 2013;14(9):901-908. Epub 2013 Jul 16.

Damron TA, Ward WG, Stewart A. Osteosarcoma, chondrosarcoma, and Ewing's sarcoma: National Cancer Data Base Report. *Clin Orthop Relat Res*. 2007;459:40-47.

Engels EA, Fraumeni Jr JF. New Malignancies Following Cancer of the Bone and Soft Tissue, and Kaposi Sarcoma. In: Curtis RE, Freedman DM, Ron E, Ries LAG, Hacker DG, Edwards BK, Tucker MA, Fraumeni JF Jr. (eds). New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000. National Cancer Institute. NIH Publ. No. 05-5302. Bethesda, MD, 2006. Accessed on 4/18/2014 at http://seer.cancer.gov/archive/publications/mpmono/MPMonograph_complete.pdf.

Gebhardt MC, Springfield D, Neff JR. Sarcomas of bone. In: Abeloff MD, Armitage JO, Lichter AS, Niederhuber JE. Kastan MB, McKenna WG, eds. *Clinical Oncology*. 4th ed. Philadelphia, Pa.: Elsevier; 2008: 2471-2572.

Gelderblom H, Hogendoorn PC, Dijkstra SD, et al. The clinical approach towards chondrosarcoma. *Oncologist*. 2008;13:320-329.

Giuffrida AY, Burgueno JE, Koniaris LG, et al. Chondrosarcoma in the United States (1973 to 2003): an analysis of 2890 cases from the SEER database. *J Bone Joint Surg Am*. 2009;91(5):1063-1072.

Hansen MF, Seton M, Merchant A. Osteosarcoma in Paget's disease of bone. *J Bone Miner Res*. 2006;21 Suppl 2:P58-63.

Lewis DR, Ries LAG. Cancers of the bone and joint. In, Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program, NIH Pub. No. 07-6215, Bethesda, MD, 2007.

Malawer MM, Helman LJ, O'Sullivan B. Sarcomas of bone. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. 9th ed. Philadelphia, Pa.: Lippincott Williams & Wilkins; 2011: 1578-1609.

National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Bone Cancer. Version 1.2014. Accessed at www.nccn.org on January 6, 2014.

Online Mendelian Inheritance in Man, OMIM (TM). McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD). Accessed at http://omim.org/ on October 11, 2012.

Springfield D, Rosen G. Bone tumors. In: Kufe DW, Bast RC, Hait WN, Hong WK, Pollock RE, Weichselbaum RR, Holland JF, Frei E, eds. *Cancer Medicine*, 7th ed. Hamilton, Ontario: BC Decker; 2006: 1675-1693.

Stacchiotti S, Marrari A, Tamborini E, et al. Response to imatinib plus sirolimus in advanced chordoma. *Ann Oncol*. 2009;20(11):1886-1894.

Stacchiotti S, Longhi A, Ferraresi V, et al. Phase II study of imatinib in advanced chordoma. *J Clin Oncol*. 2012;30(9):914-920. Epub 2012 Feb 13.

Stacchiotti S, Tamborini E, Lo Vullo S, et al. Phase II study on lapatinib in advanced EGFR-positive chordoma. *Ann Oncol*. 2013;24(7):1931-1936. Epub 2013 Apr 4.

Tarpey PS, Behjati S, Cooke SL, et al. Frequent mutation of the major cartilage collagen gene COL2A1 in chondrosarcoma. *Nat Genet*. 2013;45(8):923-926. Epub 2013 Jun 16.

Thomas DM, Skubitz KM. Giant cell tumour of bone. *Curr Opin Oncol*. 2009;21(4):338-344.

Thomas D, Henshaw R, Skubitz K, et al. Denosumab in patients with giant-cell tumour of bone: an open-label, phase 2 study. *Lancet Oncol*. 2010;11(3):275-280.

Walcott BP, Nahed BV, Mohyeldin A, et al. Chordoma: current concepts, management, and future directions. *Lancet Oncol*. 2012;13(2):e69-76.

Last Medical Review: 3/21/2014
Last Revised: 1/21/2016

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