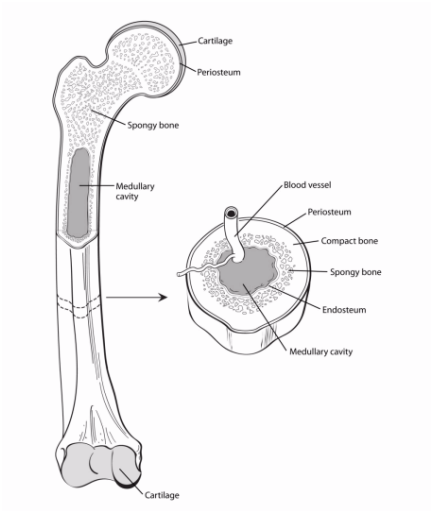
Bone Cancer

What is bone cancer?

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*.

CAUSES, RISK FACTORS, AND PREVENTION

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.

EARLY DETECTION, DIAGNOSIS, AND STAGING

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.

TREATING BONE CANCER

How is bone cancer treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

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?"

TALKING WITH YOUR DOCTOR

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*.

AFTER TREATMENT

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 withchemotherapy, 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.

WHAT`S NEW IN BONE CANCER RESEARCH?

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.

Source: American Cancer Society®