



# Castleman Disease

## What is Castleman disease?

Castleman disease (CD) is a disease of lymph nodes and related tissues. It was first described by Dr. Benjamin Castleman in 1956. It was previously called *Castleman's disease*. CD is also known as *giant lymph node hyperplasia* and *angiofollicular lymph node hyperplasia*.

CD is not officially a cancer, but the multicentric form of this disease acts very much like lymphoma (cancer of lymph nodes). In fact, many people with this disease eventually develop lymphomas. This is why it is included in the American Cancer Society's cancer information. (For information about lymphoma, see our documents, *Hodgkin Disease* and *Non-Hodgkin Lymphoma*.)

Instead of being called a cancer, CD is often called a *lymphoproliferative disorder*. This means there is an abnormal overgrowth of cells of the lymph system that is similar in many ways to lymphomas. Like lymphoma, CD is often treated with chemotherapy or radiation therapy.

## About lymph nodes and lymphoid tissue

To understand Castleman disease, it helps to know about the body's lymph system.

Lymphoid tissue, also known as *lymphatic tissue*, is the main part of the immune system. It is formed by different types of cells that work together to help the body fight infections. The main cells in lymphoid tissue are lymphocytes, a type of white blood cell. There are 2 main types of lymphocytes: B cells and T cells.

Lymphoid tissue is found in many places throughout the body, including:

- Lymph nodes: bean-sized collections of lymphocytes found in small groups throughout the body, including inside the chest, abdomen, and pelvis. They can sometimes be felt under the skin in the neck, under the arms, and in the groin.

- **Thymus:** a small organ behind the upper part of the breastbone and in front of the heart. The thymus plays a vital role in development of T cells.
- **Spleen:** an organ under the lower part of the rib cage on the left side of the body. The spleen makes lymphocytes and other immune system cells to help fight infection. It also stores healthy blood cells and helps filter the blood.
- **Tonsils and adenoids:** collections of lymphoid tissue at the back of the throat. They help protect the body against germs that are breathed in or swallowed.
- **Bone marrow:** the soft inner part of certain bones that makes red blood cells, blood platelets, and white blood cells (including lymphocytes).
- **Digestive tract:** the stomach, intestines, and other organs, which also have lymphoid tissue.

## Types of Castleman disease

The 2 main forms of CD are called *localized* and *multicentric*. They affect people very differently.

### **Localized (Unicentric) Castleman disease**

Localized CD only affects a single group of lymph nodes. It is not widespread. Lymph nodes in the chest or abdomen are affected most often. CD causes these lymph nodes to enlarge. These abnormally large lymph nodes may press on other organs and tissues inside the chest or abdomen.

Enlarged lymph nodes in the chest can press on the windpipe (trachea) or smaller breathing tubes (bronchi), causing breathing problems. If the enlarged nodes are in the abdomen, the person might feel pain or pressure in that area. Sometimes the enlarged nodes are in places such as the neck, groin, or underarm area and are first noticed as a lump under the skin.

People with localized CD are usually cured when the affected lymph nodes are removed with surgery.

### **Multicentric Castleman disease**

Multicentric CD affects more than a single group of lymph nodes. It can also affect other organs containing lymphoid tissue. This form sometimes occurs in people infected with human immunodeficiency virus (HIV), the virus that causes AIDS. Multicentric CD is more serious than the localized type, particularly in people with HIV infection.

People with multicentric CD often have problems such as serious infections, fevers, weight loss, fatigue, night sweats, and nerve damage that can cause weakness and numbness. Blood tests often show too few red blood cells (anemia) and high levels of antibodies in the blood (hypergammaglobulinemia).

CD can weaken the immune system severely, making it hard to fight infection. Infections in people with multicentric CD can be very serious and may even lead to death. CD also increases the risk of developing lymphoma, a cancer of lymphoid tissue. This can be fatal.

## Microscopic subtypes of Castleman disease

Castleman disease can also be classified based on how the lymph node tissue appears under a microscope. These are called microscopic subtypes.

- The **hyaline vascular** type is most common. It tends to be localized, but in rare cases it is multicentric.
- The **plasma cell** type is slightly more likely to be multicentric, but it is sometimes localized.
- The **mixed** subtype shows areas of both types. It occurs less often.

In choosing treatments, doctors believe that the microscopic type is less important than whether the disease is localized or multicentric.

## What are the key statistics about Castleman disease?

We don't know how many people are diagnosed with Castleman disease (CD) each year. The National Cancer Institute has a program that keeps track of how many people have each type of cancer, but because CD is not a cancer it is not included in this program.

We do know that CD is rare, especially in people who are otherwise healthy. It is much more likely to occur in people infected with HIV. Over the past 20 years, as the number of people with HIV infection has increased, the number of people diagnosed with CD has also been increasing. Modern anti-viral treatments have helped people with HIV live much longer, but these drugs do not seem to lower the chance of getting CD.

CD can affect children as well as adults. Younger people are more likely to have the localized form. Older adults and those with HIV infection are more likely to have the multicentric form.

## What are the risk factors for Castleman disease?

A risk factor is anything that might change a person's chance of getting a disease. But risk factors don't tell us everything. Having a risk factor, or even several, does not mean that you will get the disease. Having few or no risk factors doesn't mean you won't get the disease.

Most patients with Castleman disease (CD) have no known risk factors.

Infection with HIV is the only clear-cut risk factor for CD. Castleman disease is much more common in people with this infection, particularly in those who have developed the acquired immunodeficiency syndrome (AIDS).

## Do we know what causes Castleman disease?

The main feature of Castleman disease is an overgrowth of lymphocytes (immune cells) called B cells. The cause of Castleman disease (CD) is not known for sure, but doctors suspect it is related to problems with the way a person's immune system is working. Many people with CD have abnormally high blood levels of certain substances produced by immune system cells.

Some scientists believe that some cases of CD may be caused by the body making too much of a protein called interleukin-6 (IL-6). IL-6 normally helps regulate immune function. Too much IL-6 seems to cause lymphocytes to grow and divide too quickly. High levels of IL-6 are often seen in the multicentric form of CD. But it's not clear what causes the high levels of IL-6.

A virus seems to be involved in at least some cases of CD. Human herpes virus type 8 (HHV-8) is found in the lymph node B cells of many people who are HIV-positive and have multicentric CD. This virus is also known as Kaposi sarcoma-related herpes virus (KSHV) because it has also been found in people with Kaposi sarcoma (a rare type of cancer). In fact, some people with CD also have Kaposi sarcoma. HHV-8 has also been shown to cause infected cells to make a form of IL-6.

## How is Castleman disease diagnosed?

People with Castleman disease (CD) may see their doctor because they have felt a lump that hasn't gone away, they develop some of the other symptoms listed below, or they just don't feel well and go in for a checkup.

CD is rare, and its symptoms are often like those caused by other diseases (including infections and lymphomas), so doctors may suspect it is something else at first. The actual diagnosis of CD is made when doctors remove an affected lymph node and look at it under a microscope. This procedure, known as a *biopsy*, is described below.

## Signs and symptoms of CD

For most people with the localized form of CD, an enlarged lymph node, usually inside the chest or abdomen, is often the only sign of the disease. If the enlarged node is near the skin it might be seen or felt, but if it is in the chest or abdomen it may not be noticed until it grows large enough to cause other symptoms.

If the enlarged node is in the chest, it may press on the windpipe. A person may have trouble breathing, a cough, or a feeling of fullness in the chest. CD in the abdomen can

cause trouble eating, pain, or just a feeling of fullness. In general, most people with localized CD feel well otherwise, although some may also have some of the other symptoms listed below.

People with multicentric CD have more than one area of enlarged lymph nodes. The involved nodes may be in the chest or abdomen, but multicentric CD disease often affects lymph nodes in the groin, the underarm area, and on the sides of the neck, which can often be seen or felt as lumps under the skin.

Multicentric CD can also affect lymphoid tissue of internal organs, causing the liver, spleen, or other organs to enlarge. Enlarged organs may be seen or felt as masses under either side of the rib cage. They may also add to problems eating or a sense of fullness in the abdomen.

In addition, people with either type of CD may have other symptoms. But these symptoms occur much more often in people with multicentric than localized CD.

The most common include:

- Fever
- Weakness and fatigue (tiredness)
- Night sweats (that soak the sheets)
- Weight loss
- Loss of appetite
- Nausea and vomiting
- Nerve damage that leads to numbness and weakness (neuropathy)
- Leg swelling (edema)
- Skin rashes

*Amyloidosis*, a condition where abnormal proteins build up in tissues around the body, can occur in CD. This can lead to kidney damage, heart damage, nerve damage, and intestinal problems, mainly diarrhea. If the CD is successfully treated, the amyloidosis often improves or even goes away.

*Anemia* (low red blood cell counts) is very common in multicentric CD, and can lead to problems with weakness and shortness of breath.

## Medical history and physical exam

If your symptoms suggest you might have a lymph node problem such as CD, your doctor will want to get a thorough medical history, including information about your symptoms, possible risk factors, family history, and other medical conditions.

Next, the doctor will examine you, paying special attention to the lymph nodes and other areas of the body that might be involved, including the spleen and liver. Because infections are the most common cause of enlarged lymph nodes, the doctor will look for an infection in the part of the body near the swollen lymph nodes.

The doctor may also order blood tests to check for infections or other problems. Several types of blood tests may be abnormal in people with CD.

If the doctor suspects that CD or another serious problem (such as lymphoma) might be causing the symptoms, he or she may order imaging tests, and/or do a biopsy of an affected lymph node (see below).

## Imaging tests

Imaging tests use x-rays, magnetic fields, or radioactive particles to produce pictures of the inside of the body. These tests may be done for a number of reasons, including looking for enlarged lymph nodes or other problems that might be causing symptoms, looking for enlarged nodes in other parts of the body, and helping determine whether treatment has been effective.

People who might have CD (or another lymph node problem) may have one or more of the following tests.

### **Computed tomography (CT) scan**

The CT scan is an x-ray test that produces detailed cross-sectional images of your body. Unlike a regular x-ray, CT scans can show the detail in soft tissues (such as internal organs). This scan can help tell if any lymph nodes or organs in your body are enlarged.

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

Before the scan you may be asked to drink 1 or 2 pints of a contrast agent. This helps outline the intestine so that certain areas are not mistaken for tumors. You may also need an intravenous (IV) 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, especially in the face). Some people are allergic to the dye and get hives or, rarely, more serious reactions like trouble breathing and low blood pressure. You can be given medicine to prevent and treat allergic reactions. Be sure to tell your doctor if you have any allergies or have ever had a reaction to any contrast material used for x-rays.

CT scans take longer than regular x-rays because you need to lie still on a table while they are being done. During the test, the table slides in and out of the scanner, a ring-shaped machine that completely surrounds the table. You might feel a bit confined by the ring you lie within while the pictures are being taken.

CT scans can also be used to guide a biopsy needle precisely into an enlarged lymph node. For this procedure, called a *CT-guided needle biopsy*, you remain on the CT scanning table while a doctor moves a biopsy needle through the skin and toward the location of the lymph node. CT scans are repeated until the needle is within the lymph node. A fine needle biopsy sample (tiny fragments of tissue) or a core needle biopsy sample (a larger cylinder of tissue) is removed to be looked at under a microscope. While a needle biopsy cannot accurately diagnose CD by itself, it can sometimes help diagnose or exclude other diseases that can cause large lymph nodes.

## **Magnetic resonance imaging (MRI)**

This test is not used as often as CT scans for lymph node problems, but if your doctor is concerned about areas near the spinal cord or brain, MRI is very useful for looking at these areas.

MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into a very detailed image of parts of the body. A contrast material might be injected just as with CT scans but is used less often.

MRI scans they take longer than CT scans – often up to an hour. You have lie inside a narrow tube, which is confining and can upset people with a fear of enclosed spaces. Newer, more open MRI machines may be another option. The MRI machine makes loud buzzing and clicking noises that you may find disturbing. Some places provide headphones or earplugs to help block this noise out.

## **Chest x-ray**

This may be done to find out whether there are enlarged lymph nodes in your chest – usually in the center part between the lungs called the *mediastinum*.

## **Ultrasound**

Ultrasound uses sound waves and their echoes to produce a picture of internal organs or masses. For this test, a small, microphone-like instrument called a transducer is placed on the skin (which is first lubricated with a gel). It emits sound waves and picks up the echoes as they bounce off the organs. The echoes are converted by a computer into a black and white image that is displayed on a computer screen.

Ultrasound can be used to look at lymph nodes near the surface of the body or to look inside your abdomen for enlarged lymph nodes or organs such as the liver and spleen. It can also detect kidneys that have become swollen because the outflow of urine has been blocked by enlarged lymph nodes. (It can't be used to look at organs or lymph nodes in the chest because the ribs block the sound waves.)

This is an easy test to have done, and it uses no radiation. For most ultrasounds, you simply lie on a table, and a technician moves the transducer over the part of your body being looked at.

## **Positron emission tomography (PET) scan**

PET scans are helpful in finding small collections of fast-growing cells that may not be visible on CT scan. PET is not often used to diagnose CD, but sometimes it can help the doctor determine the cause of enlarged lymph nodes.

For a PET scan, a form of radioactive sugar (known as fluorodeoxyglucose or FDG) is injected into the blood. After about an hour, you are moved onto a table in the PET scanner. You lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body.

Any cancer cells in the body will be growing quickly, so they absorb large amounts of the radioactive sugar. CD cells don't take up the sugar as much as cancer cells, but they do seem to take it up more than normal cells. The picture from a PET scan is not finely detailed like a CT or MRI scan, but it can provide helpful information about your whole body.

Often the PET scan is combined with a CT scan, which is more detailed. This helps the doctor determine if abnormal areas seen on the CT scan are CD, cancer, or something else.

## **Gallium scan**

For this test, a solution containing slightly radioactive gallium is injected into a vein. It is attracted to lymph tissue in the body. A few days later a special camera is used to detect the radioactivity, showing the location of the gallium. A gallium scan can sometimes find unsuspected sites of CD disease, but it is not always reliable since the gallium may not be taken up by all of the lymph nodes affected by CD.

This test is not used as much now as in the past, as many doctors may do a PET scan instead.

## **Lymph node biopsy**

A doctor may suspect you have Castleman disease based on your symptoms or the results of exams or tests, but it can only really be diagnosed by removing the enlarged lymph node and examining it under the microscope. This procedure is called a *biopsy*. Different types of biopsies may be used, based on where the lymph node is.

**Excisional or incisional biopsy:** If the lymph node is near the skin surface, a surgeon can often remove the node using local anesthesia (numbing medicine). The surgeon makes a small incision (cut) over the enlarged lymph node, removes the node, and then stitches the incision closed. If the procedure removes the entire lymph node, it is called an *excisional biopsy*. If only part of the node is removed, it is called an *incisional biopsy*.

If the lymph node is in the chest or the abdomen, then the surgeon may need to make a large incision to get into either of these places. This is more like major surgery but it may be needed to know what is causing the lymph node to enlarge.

Sometimes, lymph nodes in the chest can be removed by *mediastinoscopy*. In this procedure, a small cut is made in the front of the neck and a thin, hollow, lighted tube (called a mediastinoscope) is inserted behind the sternum (breast bone) and in front of the windpipe to look at the area. Special instruments can be passed through this tube to remove all or part of a lymph node.

The same type of procedure can be used to sample lymph nodes in the abdomen. In this case, the test is known as *laparoscopy*. A small cut is made in the abdomen and a thin, hollow, lighted tube (called a laparoscope) is inserted to allow the doctor to look at the area and remove all or part of a lymph node.

**Fine needle aspiration (FNA) or core needle biopsy:** Sometimes lymph nodes are biopsied by putting a hollow needle into the node to remove a small amount of tissue. In a fine needle aspiration (FNA) biopsy, the doctor uses a very thin, hollow needle attached to a syringe to withdraw (aspirate) a small amount of tissue from the enlarged node. For a core needle biopsy, the doctor uses a larger needle to remove a slightly larger piece of tissue.

Doctors have found that diagnosis of CD by needle biopsy is sometimes possible, but biopsy methods that remove larger samples of tissue are usually recommended because they are thought to be more accurate.

## Lab tests of biopsy samples

All biopsy specimens are looked at under a microscope by a pathologist (a doctor who is specially trained to diagnose disease), who studies the size and shape of the cells and how they are arranged. Since this disease is so rare, the pathologist may ask another pathologist with additional training in diagnosing blood and lymph node diseases (called a *hematopathologist*) to look at the biopsy. Sometimes it is hard to tell if the lymph node is affected by CD or by lymphoma. In these cases, other tests may be done on the lymph node tissue.

**Immunohistochemistry:** In this test, a part of the biopsy sample is treated with special man-made antibodies that will attach only to cells that contain specific molecules on their surface. These antibodies cause color changes, which can be seen under a microscope. This test may help tell whether there is CD or lymphoma in the lymph node.

**Flow cytometry:** Like immunohistochemistry, this test looks for certain substances on the outside surface of cells that help show what types of cells they are. But this test can look at many more cells than immunohistochemistry.

For this test, a sample of cells is treated with special antibodies that stick to the cells only if certain substances are present on their surfaces. The cells are then passed in front of a laser beam. If the cells now have antibodies attached to them, the laser will cause them to

give off light, which can be measured and analyzed by a computer. Groups of cells can be separated and counted by these methods.

This test can help determine whether lymph node swelling is caused by lymphoma, some other cancer, or a non-cancerous disease like Castleman disease.

## How is Castleman disease staged?

When talking about cancer, the *stage* is a description of how far it has spread. The stage helps doctors determine the best treatment and the likely outlook (prognosis) for the patient. Most cancers have a formal staging system that lets doctors sum up the extent of the cancer.

Since Castleman disease (CD) is not a cancer, it doesn't have a formal staging system. Instead, doctors use other important pieces of information to help decide on the best treatment and to give them an idea of how well a patient might do.

The most important factor when deciding on treatment is whether the CD is localized/unicentric or multicentric. Localized/unicentric CD affects only a single lymph node (or lymph node group). The multicentric type affects 2 or more groups of lymph nodes in different parts of the body. It may also involve internal organs like the spleen or liver. Tests are done to see what lymph nodes and organs are affected to learn which type of CD a patient has. These tests often include some of the imaging tests mentioned earlier, such as a chest x-ray and either a CT scan or MRI of the chest and abdomen.

Another factor is the microscopic subtype of the CD, which is a description of the patterns of cells seen under the microscope in the biopsy sample. These subtypes are described in the section, "What is Castleman disease?"

A third important factor is whether or not the patient is infected with the human immunodeficiency virus (HIV), the virus that causes AIDS. Just about all people infected with HIV who develop CD will have the multicentric form of the disease. These patients are among the hardest to treat.

## Outlook (prognosis) for people with Castleman disease

Some people may want to know statistics on the outlook for those in similar situations, while others may not find the numbers helpful, or may even not want to know them. Whether or not you want to read about the statistics below for CD is up to you.

It is hard to get accurate numbers on the outlook for people with CD because it is rare. Most statistics on the disease come from small numbers of patients who were treated at a single center or hospital. These numbers might not accurately reflect the outcomes for all people with CD.

The numbers below come from a study of nearly 200 people treated for Castleman disease in many different centers. The study divided people into groups based on whether

the CD was unicentric or multicentric, its microscopic subtype, and whether the patient was infected with HIV (HIV+) or not infected (HIV-).

The 3-year disease-free survival (DFS) rate refers to the percentage of patients who were still alive and had no signs of CD at least 3 years after it was diagnosed. Of course, many people went much longer than 3 years without any signs of CD (and many were likely cured).

Type of Castleman Disease	3-Year Disease-Free Survival
Unicentric, hyaline vascular, HIV-	93%
Unicentric, plasma cell or mixed, HIV-, OR Multicentric, hyaline vascular, HIV-	79%
Multicentric, plasma cell, HIV-	46%
HIV+ (multicentric)	28%

Even when taking the factors above into account, disease-free survival rates are at best rough estimates. Your doctor can tell you how well these numbers may apply to you, as he or she is familiar with your particular situation.

## How is Castleman disease 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 health 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

Once Castleman disease (CD) has been diagnosed, your health care team will discuss treatment options with you. Several different types of treatment can be used for CD. The treatment options depend on the whether the CD is unicentric or multicentric, as well as other factors. Of course, no two patients are exactly alike, and treatment is often tailored to each patient's situation.

Based on your treatment options, you may have different types of doctors on your treatment team. These doctors may include:

- A surgeon
- A hematologist: a doctor who treats disorders of the blood and lymph system, including CD.
- A medical oncologist: a doctor who treats cancer and similar diseases with medicines.
- A radiation oncologist: a doctor who treats cancer and similar diseases with radiation therapy.

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

It is important to discuss all of your treatment options as well as their possible side effects with your doctors to help make the decision that best fits your needs. In choosing a treatment plan, consider your health and the type of CD. Be sure that you understand all the risks and side effects of the various treatments before making a decision.

CD is a rare disease, so not many doctors have much experience in treating it. If time permits, it is often a good idea to seek a second opinion. Getting a second opinion can give you more information and help you feel confident about the treatment plan that you choose. Your doctor should be willing to help you find another cancer doctor who can give you a second opinion.

The next few sections describe the types of treatment used for Castleman disease. This is followed by a discussion of the typical treatment options based on the type of CD, as well as other factors when these are important.

## Surgery for Castleman disease

Surgery is often used to obtain a tissue sample to diagnose Castleman disease (CD). A lymph node biopsy (described in “How is Castleman disease diagnosed?”) is usually a minor procedure, and patients can often go home afterwards.

Surgery also works well to treat localized (unicentric) CD. The type of surgery depends on where the disease is located.

If the involved lymph node or nodes are in a place that is easy to get to, such as in the armpit, then surgery is usually straightforward. In many cases the person may even be able to go home the same day after the surgery.

When the enlarged lymph nodes are in a place that is hard to get to, like deep in the chest or abdomen, surgery is more complex. The patient often has some pain and may need to stay in the hospital for a few days after the operation.

Aside from pain, possible side effects of surgery can include poor wound healing, bleeding at the surgery site, and infection. Depending on the site of surgery, other side effects are also possible.

## Radiation therapy for Castleman disease

Radiation therapy uses high-energy radiation to kill cells. Radiation focused from a source outside the body is called *external beam radiation*. Radiation therapy has sometimes been used instead of surgery to treat localized Castleman disease (CD). Some doctors may also use it as part of the treatment for multicentric CD.

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

Side effects of radiation therapy may vary but often include mild skin problems and fatigue. Radiation of the abdomen may cause nausea, diarrhea, and loss of appetite. These side effects tend to improve a short while after the radiation is stopped. Radiation to the chest area may damage the heart and lungs. This might eventually lead to problems such as shortness of breath or an increased risk of heart attacks. Radiation may also make the side effects of chemotherapy worse if they both are given at the same time.

## Corticosteroids for Castleman disease

Corticosteroids are a group of drugs related to hormones made in the body by the adrenal glands. These drugs inhibit the immune system, so they are useful in treating people with certain immune system diseases and cancers that develop from immune system cells, such as lymphomas. Some patients with multicentric Castleman disease (CD) are helped by treatment with these drugs.

Corticosteroids are often taken as pills, but they can also be given as an injection into a vein. Prednisone is the corticosteroid pill most often used to treat lymphoma and CD.

Side effects of corticosteroids can include increased blood sugar (which may lead to diabetes), depression, increased risk of infections, weakened bones, fatigue, muscle weakness, weight gain, fluid retention, and high blood pressure. Most of these side effects improve after the drug is stopped.

## Chemotherapy for Castleman disease

Chemotherapy (chemo) is the use of anti-cancer drugs that are injected into a vein or a muscle or are taken by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment very useful for multicentric Castleman disease (CD). Chemo may be used alone, in combination with corticosteroids, or in combination with radiation therapy (called *chemoradiation*).

Many chemo drugs have been used to treat patients with multicentric CD. The drugs used most often include carmustine, cladribine, chlorambucil, cyclophosphamide, doxorubicin, etoposide, melphalan, vinblastine, and vincristine. Often several drugs are combined.

Chemotherapy combinations like those used for lymphoma have been used. But because CD is so rare, there is not a lot of information on which chemo treatment is best or even how well it works.

Doctors give chemo in cycles, in which a period of treatment is followed by a rest period to allow the body time to recover. Each chemo cycle generally lasts for several weeks. Most chemo treatments are given on an outpatient basis (in the doctor's office or clinic or hospital outpatient department) but some may require a hospital stay. Sometimes a patient takes one drug combination for several cycles and then later is switched to a different one.

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer and diseases like CD. But other cells in the body, such as those in the bone marrow, the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemotherapy, which can lead to certain side effects.

The side effects of chemo depend on the type and dose of drugs given and the length of time they are taken. These side effects can include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea
- Increased risk of infection (due to low white blood cell counts)
- Easy bruising and bleeding (due to low platelet counts)
- Fatigue and weakness (due to anemia - low red blood cells)

Your doctor will try to avoid or lessen these side effects as much as possible. For example, drugs can be given before or along with chemotherapy to help prevent or reduce nausea and vomiting. Most side effects are temporary and go away after treatment is finished.

Infections can be very serious in people getting chemo. A low white blood cell count is an important risk factor for serious infections, so some patients find it helpful to keep track of their counts. If you are interested in this information, ask your doctor or nurse about your blood cell counts and what these numbers mean. You may want to keep a diary of your treatment and blood counts to help you follow the effects of your treatment.

If your white blood cell counts are very low during treatment, you can help reduce your risk of infection by carefully limiting your exposure to germs. During this time, your doctor may advise you to:

- Wash your hands often.

- Avoid fresh, uncooked fruits and vegetables and other foods that might carry germs.
- Avoid fresh flowers and plants because they may carry mold.
- Make sure other people wash their hands before they touch you.
- Avoid large crowds and people who are sick (wearing a surgical mask offers some protection in these situations).

Certain chemo drugs can have other, more specific side effects. Organs that could be damaged by certain chemo drugs include the kidneys, liver, testicles, ovaries, brain, heart, and lungs. Many of the drugs used to treat CD can cause nerve damage, leading to problems such as numbness and tingling in the hands and feet.

If serious side effects occur, the chemotherapy may have to be reduced or stopped, at least for a short time. Your doctor will carefully monitor and adjust drug doses because some side effects can be permanent.

## Immunotherapy for Castleman disease

Immunotherapy is treatment that either boosts the patient's own immune system or uses man-made versions of the normal parts of the immune system.

### Monoclonal antibodies

Monoclonal antibodies are special immune proteins made in the lab. They are directed toward specific molecules on the surface of cells.

Rituximab (Rituxan<sup>®</sup>) is a monoclonal antibody that is widely used for lymphoma. It can also be helpful in treating Castleman disease (CD). Rituximab attaches to a protein called CD20 that is found on the surface of some lymphocytes. This attachment tells the cell to die.

Patients get rituximab through infusion into a vein (IV) at the doctor's office or clinic. As when it is used to treat lymphoma, it is often given along with chemotherapy.

Side effects of rituximab are most common during the infusion, and can include chills, fever, nausea, rashes, fatigue, and headaches. Rarely, more severe side effects occur during the infusion, such as trouble breathing and low blood pressure. This drug may also increase a person's risk of certain infections. Unlike regular chemotherapy, rituximab does not cause low blood counts or hair loss.

In people who have ever been infected with the hepatitis B virus, this drug can sometimes cause the infection to become active again. Your doctor may check your blood for signs of a prior hepatitis infection before starting this drug to see if it is safe.

Newer antibodies that attack other targets are also being studied for use against CD. These are discussed in the section, "What's new in research and treatment of Castleman disease?"

## Thalidomide

The drug thalidomide (Thalomid<sup>®</sup>) is a type of drug called an *immunomodulating agent*. It is thought to work by affecting parts of a person's immune system, although it's not exactly clear how it does this. It is used to treat certain cancers of immune cells such as multiple myeloma and some types of lymphoma, but it has also helped some patients with CD.

Thalidomide is taken once a day as a capsule. Side effects can include drowsiness, fatigue, severe constipation, low white blood cell counts (with an increased risk of infection), and neuropathy (nerve damage causing pain). It also increases the risk of serious blood clots that start in the leg and can travel to the lungs. Because thalidomide causes severe birth defects if taken during pregnancy, this drug should not be used by women who are or may become pregnant.

## Interferon

Interferon is a hormone-like protein naturally made by white blood cells in the body to help the immune system fight infections. Some patients with CD have improved with man-made interferon treatment.

Interferon is given by an injection, either daily or several times a week. This may be into a vein (IV), under the skin (SubQ), or into a muscle (IM). It may be given in a doctor's office, or you or a family member can be taught how to give the medicine under the skin.

Side effects of this treatment can include fatigue, fever, chills, headaches, muscle and joint aches, and mood changes. Because of these side effects, interferon is not used very often. It may be given to some patients in addition to chemotherapy.

## Antiviral drugs for Castleman disease

Multicentric Castleman disease (CD) is sometimes associated with the virus HHV-8. Doctors have had some success in treating a few patients with multicentric CD with drugs that kill this virus, such as ganciclovir.

Many patients with HIV infection are treated with anti-retroviral therapy to keep the HIV in check. The effect of therapy for HIV on CD is not clear.

## Clinical trials for Castleman disease

You may have had to make a lot of decisions since you've been told you have Castleman disease (CD). One of the most important decisions you will make is choosing which treatment is best for you. You may have heard about clinical trials being done for CD. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our Web site at [www.cancer.org/clinicaltrials](http://www.cancer.org/clinicaltrials). You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at [www.cancer.gov/clinicaltrials](http://www.cancer.gov/clinicaltrials).

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the-art treatment. Sometimes they may be the only way to get access to some newer treatments. They are also the only way for doctors to learn better methods to treat CD. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our Web site or call our toll-free number (1-800-227-2345) and have it sent to you.

## Complementary and alternative therapies for Castleman disease

When you have Castleman disease (CD) you are likely to hear about ways to treat your disease or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites may offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

### **What exactly are complementary and alternative therapies?**

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

**Complementary methods:** Most complementary treatment methods are not offered as cures for CD. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not to be helpful, and a few have even been found harmful.

**Alternative treatments:** Alternative treatments may be offered as CD cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give your disease more time to grow and make it less likely that treatment will help.

## **Finding out more**

It is easy to see why people with CD may think about alternative methods. You want to do all you can to fight your disease, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating CD.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most diseases? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at.

## **The choice is yours**

Decisions about how to treat or manage your disease are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

## **Treatment of localized (unicentric) Castleman disease**

Surgery is the recommended treatment for people with localized Castleman disease (CD) whenever possible. Removing the abnormal lymph node(s) usually cures the disease. Symptoms such as fever and fatigue that are caused by the CD go away when the lymph node is removed. Relapses are rare. Radiation can also cure localized disease but it's not used as often.

Some patients with localized CD develop secondary amyloidosis, a condition in which abnormal proteins build up in the kidneys, skin, and some other organs. This protein build-up stops once the lymph node affected by CD is removed.

The outlook for localized CD is very good if the affected lymph node(s) can be removed with surgery. But sometimes the surgeon cannot safely remove all the disease. This doesn't necessarily mean it will come back. Even partial removal may help, and the disease may not grow back.

## **Treatment of multicentric Castleman disease**

Multicentric Castleman disease (CD) is usually much harder to treat than localized CD. Surgery is used to biopsy an affected lymph node to make the diagnosis, but the disease

is too widespread to remove it all with surgery. Still, some people are helped when some of the diseased tissue is removed.

There is no standard therapy for multicentric CD. No single treatment works for all patients. Several types of treatment have been shown to help some patients. But because CD is rare, it has been hard for doctors to compare different treatments against each other in clinical trials.

Doctors usually try one or a combination of treatments to try to put the disease in remission. Corticosteroids, chemotherapy, and immunotherapy may be helpful. Radiation is sometimes used. Anti-viral drugs including anti-HIV treatment may also help.

In about half of patients the disease goes away completely with treatment, at least for a time. This is less likely to happen in patients with HIV/AIDS. Even if the HIV infection is under control with drug treatment, the CD is not likely to go away.

Corticosteroids, chemotherapy, and immunotherapy may produce long remissions for some patients. In other patients, the benefit does not last long and the symptoms worsen after the course of therapy is done. Some patients may not be helped by these drugs at all.

In people whose CD is no longer responding to other treatments, some doctors may recommend high-dose chemotherapy followed by a stem cell transplant. There are a few reported cases of this being successful. This is a complex, serious, and often expensive treatment, so it is important to understand what it might entail if you are considering this option. For more on this treatment, see our document, *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants)*.

The long-term outlook (prognosis) for people with multicentric CD is often not as good as for people with localized CD. Treatment may help, but the disease often comes back within a couple of years. A major concern is that people with multicentric CD are at risk of dying from other causes, like serious infections or progression of the CD to a fast-growing form of lymphoma that is hard to treat. (For more information about lymphoma, please see our document, *Non-Hodgkin Lymphoma*).

The outlook for multicentric CD tends to be worse if the person also has HIV/AIDS. When someone is HIV-positive, treatment and outlook of CD can be complicated by Kaposi sarcoma and other AIDS-related conditions. These conditions may be less of a problem if the patient is on anti-HIV treatment.

Because multicentric CD can be hard to treat, taking part in a clinical trial of newer treatments may be a good option for some people. (See “What’s new in research and treatment of Castleman disease?” for a description of some newer treatments.)

## **What should you ask your doctor about Castleman disease?**

As you cope with Castleman disease (CD) and its treatment, we encourage you to have honest, open discussions with your doctor. Feel free to ask any question that's on your

mind, no matter how small it might seem. Here are some questions you might want to ask. Be sure to add your own questions as you think of them. Nurses, social workers, and other members of the treatment team may also be able to answer many of your questions.

- Is my CD localized or multicentric?
- Has my biopsy been reviewed by a pathologist who is an expert on CD?
- Do I also have HIV infection and AIDS? If so, how does it influence my prognosis (outlook) and treatment of CD?
- Are there other tests that need to be done before we can decide on treatment?
- Are there other doctors I need to see?
- How much experience do you have treating CD?
- Should I get a second opinion before starting treatment? Can you suggest someone?
- What treatment choices do I have? Do we need to start treatment right away?
- Which treatment do you recommend, and why?
- What side effects are there to the treatments that you recommend?
- What can I do to help reduce the side effects I may have from the treatment?
- What should I do to be ready for treatment?
- How long will treatment last? What will it involve? Where will it be done?
- How will treatment affect my daily activities?
- What is my outlook for survival?
- What are the chances of the CD coming back with these treatment plans?
- What would we do if the treatment doesn't work or if the CD recurs?
- What type of follow-up will I need after treatment?
- Am I eligible for clinical trials of any new treatments?

Along with these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so that you can plan your work or activity schedule.

# What happens after treatment for Castleman disease?

For many people with Castleman disease (CD), treatment may remove or destroy the disease. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about the CD growing or coming back. (When the disease comes back after treatment, it is called *recurrence*.) This is a very common concern in people with serious diseases such as CD.

For some people, the CD may never go away completely. These people may get regular treatments with chemotherapy, corticosteroids, or other therapies to help keep the CD in check for as long as possible. Learning to live with CD as a more of a chronic disease can be difficult and very stressful. It has its own type of uncertainty.

## Follow-up care

If you have completed treatment, frequent follow-up exams are very important for several years after the treatment is finished. The doctors will continue to watch you for signs of recurrent disease, as well as for short-term and long-term side effects of treatment. It is important that you report any new symptoms to the doctor right away, so that relapse or side effects can be treated.

Checkups usually include careful physical exams, imaging tests such as CT scans when needed, and lab tests to look for signs of CD or treatment side effects.

Almost any type of treatment can have side effects. Some may last for a few weeks to months, but others can last the rest of your life. This is the time for you to talk to your health care team about any changes or problems you notice and any questions or concerns you have.

CD may recur (come back) in some people. Multicentric CD may come back as soon as the first year after treatment. If the CD does recur at some point, further treatment will depend on what treatments you've had before, how long it's been since treatment, and your health.

Some people with multicentric CD (especially those who are HIV-positive) may develop non-Hodgkin lymphoma or Kaposi sarcoma at some point. These cancers can be hard to treat, so it helps to diagnose and treat them as early as possible.

## What's new in research and treatment of Castleman disease?

Research into the causes and treatment of Castleman disease (CD) is being done in many medical centers throughout the world. Unfortunately, research into this disease is slowed by the fact that CD is so rare. Still, researchers have begun to study several promising new drugs in recent years for use against CD.

Many patients with multicentric CD have high levels of a protein called interleukin-6 (IL-6). Drugs against IL-6 have been developed and are being tested in CD. One of these drugs, tocilizumab (Actemra<sup>®</sup>), is a monoclonal antibody that blocks the action of IL-6 by binding to its receptor on lymphocytes. This drug is approved to treat rheumatoid arthritis in the United States, but some doctors may use it to treat CD as well.

Another monoclonal antibody, siltuximab, targets IL-6 itself. This drug has shown very promising results in an early study against CD, but it is only available through clinical trials at this time.

It is unclear how helpful these drugs may be in CD patients who are HIV-positive, since few HIV-positive patients have been in the studies so far. Still, these drugs may offer the best hope for the future treatment of CD.

Other drugs being studied for treatment of CD include:

- Sirolimus (Rapamune<sup>®</sup>): This drug suppresses the immune system by keeping lymphocytes in check. It is often used to help prevent the rejection of organ transplants, but it may also be helpful in CD.
- Suramin: This drug is thought to work by stopping IL-6 from attaching to and affecting lymphocytes.
- CX-4945: This drug blocks CK2, a protein that helps some cells grow and divide. It is still in the earliest phases of testing.

## **Additional resources for Castleman disease**

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

The following information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800- 227-2345.

Clinical Trials: What You Need to Know

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

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

Non-Hodgkin Lymphoma

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

*American Cancer Society Complete Guide to Complementary & Alternative Cancer Therapies*

*American Cancer Society Complete Guide to Family Caregiving, Second Edition*

## National organizations and Web sites\*

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

### **National Organization for Rare Disorders (NORD)**

Phone number: 1-203-744-0100

Toll-free number: 1-800-999-6673 (voicemail only)

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

### **International Castleman's Disease Organization**

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

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

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Last Medical Review: 6/11/2012

Last Revised: 6/11/2012

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