



Leukemia--Chronic Lymphocytic

What is cancer?

The body is made up of hundreds of millions of living cells. Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called benign. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

What is chronic lymphocytic leukemia?

Chronic lymphocytic leukemia (CLL) is a type of cancer that starts from white blood cells (called lymphocytes) in the bone marrow. It then invades the blood. Leukemia cells tend to build up in the body over time, but in many cases people don't have any symptoms for at least a few years. In time, it can also invade other parts of the body, including the lymph nodes, liver, and spleen. Compared to other types of leukemia, CLL usually grows slowly.

Doctors have found that there seem to be 2 different kinds of CLL:

- One kind of CLL grows very slowly and rarely needs to be treated. People with this kind of CLL survive an average of 15 years or more.
- The other kind of CLL grows faster and is a more serious disease. People with this form of CLL survive an average of about 8 years.

The leukemia cells from these 2 types look alike, but lab tests can tell the difference between them. The tests look for proteins called ZAP-70 and CD38. Patients whose CLL cells contain low amounts of ZAP-70 and CD38 have a better prognosis (outlook).

Leukemia is different from other types of cancer that start in organs such as the lungs, colon, or breast and then spread to the bone marrow. Cancers that start elsewhere and then spread to the bone marrow are not leukemia.

Normal bone marrow, blood, and lymphoid tissue

To understand the different types of leukemia, it helps to know some basic facts about the blood and lymph systems.

Bone marrow

Bone marrow is the soft inner part of some bones such as the skull, shoulder blades, ribs, pelvis, and backbones. The bone marrow is made up of a small number of blood stem cells, more mature blood-forming cells, fat cells, and supporting tissues that help cells grow.

Blood stem cells go through a series of changes to make new blood cells. During this process, the cells develop into either *lymphocytes* (a kind of white blood cell) or other blood-forming cells. The blood-forming cells can develop into 1 of the 3 main types of blood cell components:

- Red blood cells
- White blood cells (other than lymphocytes)
- Platelets

Red blood cells

Red blood cells carry oxygen from the lungs to all other tissues in the body, and take carbon dioxide back to the lungs to be removed. Anemia (having too few red blood cells in the body) typically causes a person to feel tired, weak, and short of breath because the body tissues are not getting enough oxygen.

Platelets

Platelets are actually cell fragments made by a type of bone marrow cell called the megakaryocyte. Platelets are important in plugging up holes in blood vessels caused by cuts or bruises. A shortage of platelets is called *thrombocytopenia*. A person with thrombocytopenia may bleed and bruise easily.

White blood cells

White blood cells help the body fight infections. Lymphocytes are one type of white blood cell. The other types of white blood cells are granulocytes (neutrophils, basophils, and eosinophils) and monocytes.

Lymphocytes: These are the main cells that make up lymphoid tissue, a major part of the immune system. Lymphoid tissue is found in lymph nodes, the thymus gland, the spleen, the tonsils and adenoids, and is scattered throughout the digestive and respiratory systems and the bone marrow.

Lymphocytes develop from cells called *lymphoblasts* to become mature, infection-fighting cells. The 2 main types of lymphocytes are known as B lymphocytes (B cells) and T lymphocytes (T cells).

- B lymphocytes protect the body from invading germs by developing (maturing) into plasma cells, which make proteins called antibodies. The antibodies attach to the germs (bacteria, viruses, and fungi), which helps other white blood cells called granulocytes to recognize and destroy them. B lymphocytes are the cells that most often develop into chronic lymphocytic leukemia (CLL) cells.
- T lymphocytes can recognize cells infected by viruses and directly destroy these cells.

Granulocytes: These are white blood cells that have granules in them. Granules are spots that can be seen under the microscope. They contain enzymes and other substances that can destroy germs, such as bacteria. The 3 types of granulocytes -- *neutrophils*, *basophils*, and *eosinophils* -- are distinguished by the size and color of their granules. Granulocytes develop from blood-forming cells called *myeloblasts* to become mature, infection-fighting cells.

Monocytes: These white blood cells, which are related to granulocytes, also are important in protecting the body against bacteria. They start in the bone marrow as blood-forming *monoblasts* and develop into mature monocytes. After circulating in the bloodstream for about a day, monocytes enter body tissues to become *macrophages*, which can destroy some germs by surrounding and digesting them. Macrophages also help lymphocytes recognize germs and start making antibodies to fight them.

Any of the blood-forming or lymphoid cells from the bone marrow can turn into a leukemia cell. Once this change takes place, the leukemia cells fail to go through their normal process of maturing. Most leukemia cells may reproduce quickly, but often the problem is that they don't die when they should. They survive and build up in the bone marrow. Over time, these cells spill into the bloodstream and spread to other organs, where they can prevent other cells in the body from functioning normally.

Types of leukemia

Not all leukemias are the same. Leukemias are divided into 4 main types. Knowing the specific type of leukemia helps doctors better predict each patient's prognosis (outlook) and select the best treatment.

Acute leukemia versus chronic leukemia

The first factor in classifying leukemia is whether most of the abnormal cells are mature (look like normal white blood cells) or immature (look more like stem cells).

In *acute* leukemia, the bone marrow cells cannot mature properly. Immature leukemia cells continue to reproduce and build up. Without treatment, most patients with acute leukemia would live only a few months. Some types of acute leukemia respond well to treatment, and many patients can be cured. Other types of acute leukemia have a less favorable outlook.

In *chronic* leukemia, the cells can mature partly but not completely. These cells may look fairly normal, but they are not. They generally do not fight infection as well as normal white blood cells do. And they survive longer, build up, and crowd out normal cells.

Chronic leukemias tend to develop over a longer period of time, and most patients can live for many years. But chronic leukemias are generally harder to cure than acute leukemias.

Myeloid leukemia versus lymphocytic leukemia

The second factor in classifying leukemia is the type of bone marrow cells that are affected.

Leukemias that start in early forms of myeloid cells -- white blood cells (other than lymphocytes), red blood cells, or platelet-making cells (megakaryocytes) -- are *myeloid* leukemias (also known as myelocytic, myelogenous, or non-lymphocytic leukemias).

If the cancer starts in lymphocytes, it is called *lymphocytic* leukemia (also known as lymphoid or lymphoblastic leukemia). Lymphomas are also cancers that start in lymphocytes. While lymphocytic leukemias develop from cells in the bone marrow, lymphomas develop from cells in lymph nodes or other organs.

By considering whether leukemias are acute or chronic, and whether they are myeloid or lymphocytic, they can be divided into 4 main types:

- Acute myeloid (or myelogenous) leukemia (AML)
- Chronic myeloid (or myelogenous) leukemia (CML)
- Acute lymphocytic (or lymphoblastic) leukemia (ALL)
- Chronic lymphocytic leukemia (CLL)

Rarer forms of lymphocytic leukemia

Along with the common form of CLL (which starts in B lymphocytes), there are some rare types of leukemia that share some features with CLL.

Prolymphocytic leukemia (PLL): This is a type of leukemia in which the cancer cells are similar to normal cells called prolymphocytes -- immature forms of B lymphocytes (B-PLL) or T lymphocytes (T-PLL). Both B-PLL and T-PLL tend to be more aggressive than the usual type of CLL. Most cases will respond to some form of treatment, but over time they tend to relapse. PLL may develop in someone who already has CLL (in which case it tends to be more aggressive), but it can also occur in people who have never had CLL.

Large granular lymphocyte (LGL) leukemia: This is another rare form of chronic leukemia. The cancer cells are large and have features of either T lymphocytes or natural killer (NK) cells (another type of lymphocyte). Most LGL leukemias are slow-growing, but a small number are more aggressive. Drugs that suppress the immune system may be helpful, but aggressive cases are very hard to treat.

Hairy cell leukemia (HCL): This is another cancer of lymphocytes that tends to progress slowly. It accounts for about 2% of all leukemias. The cancer cells are a type of

B lymphocyte but are different from those seen in CLL. There are also important differences in symptoms and treatment. This type of leukemia gets its name from the way the cells look under the microscope -- they have fine projections on their surface that make them look "hairy." Treatment for HCL can be very effective and is described in the section, "How is chronic lymphocytic leukemia treated?"

The rest of this document focuses mainly on CLL in adults, with some limited information on hairy cell leukemia. For information on other types of leukemia in adults and children, please see our separate documents on these topics.

What are the key statistics for chronic lymphocytic leukemia?

The American Cancer Society's most recent estimates for leukemia in the United States are for 2010:

- About 43,050 new cases of leukemia and about 21,840 deaths from leukemia (all kinds)
- About 14,990 new cases of chronic lymphocytic leukemia (CLL)
- About 4,390 deaths from CLL

CLL accounts for about one-third of all leukemias. The average person's lifetime risk of getting CLL is about 1/2 of 1% (about 1 in 200). The risk is slightly higher in men than in women. Factors such as having a family history of CLL may raise this risk.

CLL mainly affects older adults. The average age at the time of diagnosis is around 72 years. It is rarely seen in people under age 40, and is extremely rare in children.

What are the risk factors for chronic lymphocytic leukemia?

A risk factor is something that affects a person's chance of getting a disease such as cancer. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for a number of cancers.

But risk factors don't tell us everything. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And many people who get the disease may not have had any known risk factors. Even if a person has a risk factor and develops cancer, it is often very hard to know how much that risk factor may have contributed to the cancer.

There are very few known risk factors for chronic lymphocytic leukemia (CLL).

Certain chemical exposures

Some studies have linked exposure to Agent Orange, an herbicide used during the Vietnam War, to an increased risk of CLL. Some other studies have suggested that farming and long-term exposure to some pesticides may be linked to an increased risk of CLL, but more research in this area is needed.

Family history

First-degree relatives (parents, siblings, or children) of CLL patients have a 2- to 4-fold increased risk for this cancer.

Gender

CLL is slightly more common in males than females, but the reasons for this are not known.

Race/ethnicity

CLL is more common in North America and Europe than in Asia. Most experts think this is related to genetic differences rather than environmental factors because people keep the same risk even when they move from one area to another.

There are no other proven risk factors for CLL. The risk of getting CLL does not seem to be affected by smoking, diet, exposure to radiation, or infections.

Do we know what causes chronic lymphocytic leukemia?

The exact cause of most cases of chronic lymphocytic leukemia (CLL) is not known. But scientists have learned a great deal about the differences between normal lymphocytes and CLL cells in recent years.

Normal human cells grow and function based mainly on the information contained in each cell's chromosomes. Chromosomes are long molecules of DNA in each cell. DNA is the chemical that carries our genes -- the instructions for how our cells function. We resemble our parents because they are the source of our DNA. But our genes affect more than the way we look.

Each time a cell prepares to divide into 2 new cells, it must make a new copy of the DNA in its chromosomes. This process is not perfect, and errors can occur that may affect genes within the DNA.

Some genes contain instructions for controlling when our cells grow and divide. Certain genes that promote cell growth and division are called *oncogenes*. Others that slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*.

Cancers can be caused by DNA mutations (changes) that turn on oncogenes or turn off tumor suppressor genes.

Each human cell contains 23 pairs of chromosomes. In most cases of CLL, a change can be found in at least one of these chromosomes. Most often this change is a deletion -- that is, loss of part of a chromosome. The loss of part of chromosome 13 is the most common deletion, but other chromosomes such as 11 and 17 can also be affected. Sometimes there is an extra chromosome 12 (*trisomy 12*). Other, less common abnormalities may also be found. Scientists know these chromosome changes are important in CLL, but it's not yet clear which genes they involve or exactly how they lead to leukemia.

We do know that normal B lymphocytes are part of the immune system. They are programmed to grow and divide when they come into contact with a foreign substance called an *antigen*. (Scientists call substances *foreign* if they don't normally occur in a person's body and can be recognized by their immune system. Germs contain foreign antigens. So do blood cells from someone else with a different blood type.) Scientists think that CLL begins when B lymphocytes continue to divide without restraint after they have reacted to an antigen. But why this happens is not yet known.

Sometimes people inherit DNA mutations from a parent that greatly increase their risk of getting certain types of cancer. But inherited mutations rarely cause CLL. DNA changes related to CLL usually occur during the person's lifetime, rather than having been inherited before birth.

Can chronic lymphocytic leukemia be prevented?

Many types of cancer can be prevented by lifestyle changes to avoid certain risk factors, but there are very few known risk factors for chronic lymphocytic leukemia (CLL), and most of these cannot be avoided. Most CLL patients have no known risk factors, so there is no way to prevent these cancers.

Can chronic lymphocytic leukemia be found early?

The American Cancer Society recommends screening tests for certain cancers in people without any symptoms, because they are easier to treat if found early. But at this time, no screening tests are routinely recommended to detect chronic lymphocytic leukemia (CLL) early.

CLL is sometimes found on routine blood tests done for other reasons. For instance, a person's white blood cell count may be very high, even though he or she doesn't have any symptoms.

It is important to report any symptoms that could be caused by CLL to the doctor right away. The symptoms of CLL are discussed in the next section, "How is chronic lymphocytic leukemia diagnosed?"

How is chronic lymphocytic leukemia diagnosed?

Certain signs and symptoms might suggest that a person has chronic lymphocytic leukemia (CLL), but tests are needed to confirm the diagnosis.

Many people with CLL do not have any symptoms when it is diagnosed. The leukemia is often found when their doctor orders blood tests for some unrelated health problem or during a routine checkup.

Signs and symptoms

Even when people with CLL have symptoms, they are often vague and non-specific. Symptoms can include the following:

- Weakness
- Feeling tired
- Weight loss
- Fever
- Night sweats
- Enlarged lymph nodes (felt as lumps under the skin)
- Pain or a sense of "fullness" in the belly (especially after eating a small meal), which is caused by an enlarged spleen

Many of the signs and symptoms of advanced CLL occur because the leukemia cells replace the bone marrow's normal blood-making cells. As a result, people do not make enough red blood cells, properly functioning white blood cells, and blood platelets.

- *Anemia* is a shortage of red blood cells. It can cause tiredness, weakness, and shortness of breath.
- A shortage of normal white blood cells (*leukopenia*) increases the risk of infections. A common term you may hear is *neutropenia*, which refers specifically to low levels of neutrophils (a type of granulocyte). Although patients with CLL may have very high white blood cell counts because of excess numbers of lymphocytes (*lymphocytosis*), the leukemia cells do not protect against infection the way normal white blood cells do.

- A shortage of blood platelets (*thrombocytopenia*) can lead to excess bruising, bleeding, frequent or severe nosebleeds, and bleeding gums.

People with CLL have a higher risk of infections. This is mainly because their immune systems are not working as well as they should. CLL is a cancer of B lymphocytes, which normally make antibodies that help fight infection. But in CLL, these antibody-making cells don't work as they should, so they can't fight infections well. Infections may range from simple things like frequent colds or cold sores to pneumonia and other serious infections.

CLL may also affect the immune system in other ways. In some people with CLL, the immune system cells make abnormal antibodies that attack normal blood cells. This is known as autoimmunity. It can lead to low blood counts. If the antibodies attack red blood cells, it is known as *autoimmune hemolytic anemia*. Less often, the antibodies attack platelets and the cells that make them, leading to low platelet counts (thrombocytopenia). Rarely, the antibodies attack white blood cells, leading to leukopenia (low white blood cell counts).

CLL often causes the liver or spleen to become enlarged. If these organs are enlarged, you may notice fullness or swelling of the belly. You may also notice that you feel full after only a small meal. The spleen is on the left side, while the liver is on the right. These organs are usually covered by the lower ribs but when they are larger than normal your doctor can feel them.

CLL will often invade the lymph nodes. If the nodes are close to the surface of the body (for instance, on the sides of the neck, in the groin, in the underarm area, or above the collarbone), you or your doctor may notice the swelling as a lump under the skin. Lymph nodes inside the chest or abdomen may also become swollen, but these can be found only by imaging tests such as a computed tomography (CT) scan.

The symptoms and signs above may be caused by CLL, but they can also be caused by other conditions. Still, if you have any of these problems, it's important to see your doctor right away so the cause can be found and treated, if needed.

Medical history and physical exam

If you have any signs or symptoms that suggest you might have leukemia, your doctor will want to take a complete medical history to check for symptoms and possible risk factors. You will also be asked about your general health.

A physical exam provides information about your general health, possible signs of leukemia, and other health problems. During the physical exam, your doctor will pay close attention to your lymph nodes and other areas that might be affected.

Types of samples used to test for chronic lymphocytic leukemia

If symptoms and/or the results of the physical exam suggest you may have leukemia, the doctor will need to check samples of blood and bone marrow to be certain of this diagnosis. Other tissue and cell samples may also be taken to help guide treatment.

Blood samples

Blood samples for tests for CLL are generally taken from a vein in the arm.

Bone marrow samples

Bone marrow samples are obtained from a bone marrow aspiration and biopsy, usually at the same time. The samples are usually taken from the back of the pelvic (hip) bone, but sometimes they may be taken from the sternum (breastbone) or other bones.

In bone marrow *aspiration*, you lie on a table (either on your side or on your belly). After cleaning the skin over the hip, the doctor numbs the area and the surface of the bone with local anesthetic, which may cause a brief stinging or burning sensation. A thin, hollow needle is then inserted into the bone and a syringe is used to suck out a small amount of liquid bone marrow (about 1 teaspoon). Even with the anesthetic, most patients still have some brief pain when the marrow is removed.

A bone marrow *biopsy* is usually done just after the aspiration. A small piece of bone and marrow (about 1/16 inch in diameter and 1/2 inch long) is removed with a slightly larger needle that is twisted as it is pushed down into the bone. The biopsy may also cause some brief pain. Once the biopsy is done, pressure will be applied to the site to help prevent bleeding.

These tests are not usually needed to diagnose CLL, but they may help tell how advanced it is. They are often done before starting treatment to see how much CLL is in the bone marrow. They may then be repeated during or after treatment to see if the treatment is effective.

Lymph nodes

In an excisional lymph node biopsy, an entire lymph node is removed through a cut in the skin. If the node is near the skin surface, this is a simple operation that can be done with local anesthesia, but if the node is inside the chest or abdomen, general anesthesia (where the patient is asleep) is used.

This type of biopsy is often used to diagnose lymphomas, but it is only rarely needed in CLL. It may be used if a lymph node has grown very large and the doctor wants to know if the leukemia has changed (transformed) into a more aggressive lymphoma.

Spinal fluid

The procedure used to take samples of spinal fluid (also called cerebrospinal fluid or CSF) is called a lumbar puncture (or spinal tap). CSF is the liquid that surrounds the brain and spinal cord. For this test, the doctor first numbs an area in the lower part of the back over the spine. A small, hollow needle is then placed between the bones of the spine to withdraw some of the fluid.

This is not a routine test for patients with CLL. It is only done if the doctor suspects leukemia cells may have spread to the area around the brain or spinal cord (which is rare), or if there might be an infection in those areas.

Lab tests used to diagnose and classify leukemia

One or more of the following lab tests may be done on the samples to diagnose CLL or to help determine how advanced the disease is.

Complete blood count and blood cell exam (peripheral blood smear)

The complete blood count (CBC) is a test that measures the different cells in the blood, such as the red blood cells, the white blood cells, and the platelets. This test is often done along with a differential (or diff) which looks at the numbers of the different types of white blood cells. Patients with CLL have too many lymphocytes (called *lymphocytosis*). Having more than 10,000 lymphocytes/mm³ (per cubic millimeter) of blood makes the diagnosis almost certain, although it may need to be confirmed by the more specialized tests discussed below. The patient will often have too few red blood cells and blood platelets as well. For the peripheral blood smear, a sample of blood is looked at under the microscope. In patients with CLL, the blood smear often shows many abnormal looking lymphocytes called *smudge cells*.

Other blood tests

Other tests may be done to measure the amount of certain chemicals in the blood, but they are not used to diagnose leukemia. In patients already known to have CLL, these tests help detect liver or kidney problems caused by the spread of leukemia cells or due to the side effects of certain chemotherapy drugs. These tests also help determine if treatment is needed to correct low or high blood levels of certain minerals. If treatment with the drug rituxan (Rituximab[®]) is planned, the doctor may order blood tests to check for previous hepatitis infection (this is discussed further in the "Monoclonal antibodies" section).

Blood immunoglobulin (antibody) levels may be tested to see if the patient has enough antibodies to fight infections, especially if they have had many recent infections. Another blood protein called beta-2-microglobulin may be measured. High levels of this protein indicate a more advanced CLL.

Routine microscopic exams

Any samples taken (blood, bone marrow, lymph node tissue, or CSF) are looked at under a microscope by a pathologist (a doctor specializing in lab tests) and may be reviewed by the patient's hematologist/oncologist (a doctor specializing in blood diseases and cancer).

The doctors will look at the size, shape, and other traits of the white blood cells in the samples to classify them into specific types.

An important factor is if the cells look mature (like normal blood cells that can fight infections). Some leukemia cells can lack features of normal blood cells and are not effective in fighting infections. The most immature cells are called *lymphoblasts* (or *blasts*). Chronic lymphocytic leukemia cells usually appear mature.

A key feature of a bone marrow sample is its cellularity. Normal bone marrow contains a certain number of blood-forming cells and fat cells. Marrow with too many blood-forming cells is said to be *hypercellular*. If too few blood-forming cells are found, the marrow is called *hypocellular*. Doctors also look to see how much of the normal marrow has been replaced by CLL cells.

The pattern of spread of CLL cells in the bone marrow is also important. A pattern where the cells are in small groups (*nodular* or *interstitial* pattern) often indicates a better outlook than if the cells are scattered throughout the marrow (a *diffuse* pattern).

Cytochemistry

For cytochemistry tests, cells are exposed to chemical stains (dyes) that react with only some types of leukemia cells. These stains cause color changes that can be seen under a microscope, which can help the doctor determine what types of cells are present.

Flow cytometry

This test is important in diagnosing CLL. It looks for certain substances on the outside surface of cells that help identify what types of cells they are.

A sample of cells is treated with special antibodies that stick only to these substances. 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.

Some doctors are now using flow cytometry (or immunocytochemistry) to test for substances called ZAP-70 and CD38 on the cells. These substances seem to be linked to the type of B lymphocyte involved in the leukemia. Some recent studies suggest that CLL with fewer cells that have these substances seem to have a better outlook. These tests are still fairly new and are not available in all labs. It's not yet clear if they are accurate or helpful in all cases.

Immunocytochemistry

During this test, as in flow cytometry, cells from the blood or bone marrow samples are treated with special antibodies. But instead of using a laser and computer, the sample is treated so that certain types of cells change color when seen under a microscope.

Cytogenetics

For this test, a cell's chromosomes (pieces of DNA) are looked at under a microscope to detect any changes. Normal human cells contain 23 pairs of chromosomes, each of which is a certain size. Some cases of CLL have chromosome changes that can be seen under the microscope after the cells have been processed in a special way.

Fluorescent in situ hybridization (FISH): This is a type of cytogenetic test. It uses special fluorescent dyes that only attach to specific parts of particular chromosomes. FISH can be used to look for specific changes in chromosomes. It can be used on regular blood or bone marrow samples. It is very accurate and can usually provide results within a couple of days, which is why this test is now used in many medical centers.

In some cases of CLL, part of a chromosome may be missing. This is called a *deletion*. The most common deletions occur in parts of chromosomes 13, 11, or 17. When the leukemia cells are missing a piece of chromosome 17 (often written as del(17p)), it is linked to a poor outlook. Other, less common chromosome changes include having an extra copy of chromosome 12 (trisomy 12) or having a translocation (swapping of DNA) between chromosomes 11 and 14.

This information is sometimes helpful in determining a patient's prognosis (outlook), but it needs to be looked at along with other factors, such as the stage of CLL. The loss of part of chromosome 13 is usually linked with a slower growing disease and a better outlook, while defects in chromosomes 11 or 17 often indicate a poorer outlook. Trisomy 12 does not seem to have much of an effect on prognosis.

Imaging tests

Imaging tests use x-rays, sound waves, or magnetic fields to create pictures of the inside of the body. Imaging tests are not done to diagnose the leukemia, but they may be done for a number of reasons, including to help find a suspicious area that might be cancerous, to learn how far a cancer may have spread, and to help determine if treatment has been effective.

Computed tomography (CT) scan

The CT scan is a type of 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 test can help tell if any lymph nodes or organs in your body are enlarged. It isn't usually needed to diagnose CLL, but it may be done if your doctor suspects the leukemia is growing in an organ, like your spleen.

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 that is being studied.

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

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table moves 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 have to lay in when the pictures are being taken.

Sometimes a CT scan is combined with a PET scan in a test known as a PET/CT scan. For a PET scan, glucose (a form of sugar) containing a radioactive atom is injected into the blood. Because cancer cells in the body grow rapidly, they absorb large amounts of the radioactive sugar. A special camera can then create a picture of the areas of radioactivity in the body. The PET/CT scan combines both tests in one machine. This test allows the doctor to compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT.

Magnetic resonance imaging (MRI) scan

Like CT scans, MRI scans provide detailed images of soft tissues in the body. But 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 body tissue and by certain diseases. A computer translates the pattern into very detailed images of parts of the body. A contrast material called gadolinium is often injected into a vein before the scan to better see details. The contrast material usually does not cause allergic reactions.

MRI scans are most useful in looking the brain and spinal cord, but they are not often needed in people with CLL.

MRI scans take longer than CT scans -- often up to an hour. You may have to lie inside a narrow tube, which is confining and can be distressing to some people. 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.

Ultrasound

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

Ultrasound can be used to look at lymph nodes near the surface of the body or to look for enlarged organs inside your abdomen.

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

Chest x-ray

A plain x-ray of your chest can be done in most outpatient settings. In patients with CLL, it isn't needed for a diagnosis, but it may be used to see if you have normal lungs or if you have an infection.

How is chronic lymphocytic leukemia staged?

For most cancers, staging is the process of finding out how far the cancer has spread. Stages are often useful because they can help guide treatment and determine a person's prognosis (outlook). Most types of cancer are staged based on the size of the tumor and how far in the body the cancer has spread.

Chronic lymphocytic leukemia (CLL), on the other hand, does not usually form tumor masses. It generally involves all of the bone marrow in the body and, in many cases, has spread to other organs such as the spleen, liver, and lymph nodes when it is found. Therefore the outlook for the patient with CLL depends on other information, such as the lab test results and the results of imaging tests.

Staging for chronic lymphocytic leukemia

A staging system is a standardized way for the cancer care team to summarize information about how far a cancer has spread. There are 2 different systems for staging CLL:

- **Rai system:** This is used more often in the United States.
- **Binet system:** This is used more widely in Europe.

There are also other factors that have been found to affect prognosis, which are discussed below.

Rai staging system

The Rai system divides CLL into 5 stages:

- **Rai stage 0:** The blood lymphocyte count is too high, usually defined as over 10,000 lymphocytes/mm³ of blood (this is called *lymphocytosis*). Some doctors will diagnose CLL if the count is over 5,000/mm³ and the cells all have the same chemical pattern on special testing. The lymph nodes, spleen, and liver are not enlarged and the red blood cell and platelet counts are near normal.
- **Rai stage I:** Lymphocytosis plus enlarged lymph nodes. The spleen and liver are not enlarged and the red blood cell and platelet counts are near normal.
- **Rai stage II:** Lymphocytosis plus an enlarged spleen (and possibly an enlarged liver), with or without enlarged lymph nodes. The red blood cell and platelet counts are near normal.
- **Rai stage III:** Lymphocytosis plus anemia (too few red blood cells), with or without enlarged lymph nodes, spleen, or liver. Platelet counts are near normal.
- **Rai stage IV:** Lymphocytosis plus thrombocytopenia (too few blood platelets), with or without anemia, enlarged lymph nodes, spleen, or liver.

For practical purposes, doctors separate the Rai stages into low-, intermediate-, and high-risk groups when determining treatment options.

- Stage 0 is considered low risk.
- Stages I and II are considered intermediate risk.
- Stages III and IV are considered high risk.

These risk groups are used later in this document in the section "How is chronic lymphocytic leukemia treated?"

Binet staging system

In the Binet staging system, CLL is classified by the number of affected lymphoid tissue groups (neck lymph nodes, groin lymph nodes, underarm lymph nodes, spleen, and liver) and by whether or not the patient has anemia (too few red blood cells) or thrombocytopenia (too few blood platelets).

- **Binet stage A:** Fewer than 3 areas of lymphoid tissue are enlarged, with no anemia or thrombocytopenia.
- **Binet stage B:** 3 or more areas of lymphoid tissue are enlarged, with no anemia or thrombocytopenia.
- **Binet stage C:** Anemia and/or thrombocytopenia are present.

Both of these staging systems are helpful and have been in use for many years.

In recent years, doctors have found that other factors can also help predict a person's outlook. The factors described below are not part of formal staging systems (at least at this time), but they can also provide helpful information.

Prognostic factors for chronic lymphocytic leukemia

Along with the stage, there are other factors that help predict a person's outlook for survival. These factors are sometimes taken into account when looking at possible treatment options. Factors that tend to be linked with shorter survival time are called *adverse prognostic factors*. Those that predict longer survival are *favorable prognostic factors*.

Adverse prognostic factors

- Diffuse pattern of bone marrow involvement (more widespread replacement of normal marrow by leukemia)
- Advanced age
- Male gender
- Deletions of parts of chromosomes 17 or 11
- High blood levels of certain substances, such as beta-2-microglobulin
- Lymphocyte doubling time (the time it takes for the lymphocyte count to double) of less than 12 months
- Increased proportion of large or atypical lymphocytes in the blood
- High proportion of cells containing ZAP-70 or CD38

Favorable prognostic factors

- Non-diffuse (nodular or interstitial) pattern of bone marrow involvement
- Deletion of part of chromosome 13 (with no other chromosome abnormalities)
- Low proportion of cells containing ZAP-70 or CD38

The prognostic factors based on newer lab tests, such as the presence or absence of ZAP-70 and CD38, will probably become more important over time, and may eventually be found to be better predictors of outcome than the staging systems, particularly for people in the earliest stages of CLL.

Staging for hairy cell leukemia

There is no generally accepted staging system for hairy cell leukemia.

How is chronic lymphocytic leukemia 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.

This section starts with general comments about types of treatments used for chronic lymphocytic leukemia (CLL). This is followed by a discussion of treatment options for CLL based on risk groups.

Making treatment decisions

After the leukemia is found and staged, your cancer care team will discuss your treatment options with you. The main treatment is usually chemotherapy, but because chronic lymphocytic leukemia often grows slowly, not everyone needs to be treated right away.

It is important to take time and think about your possible choices. In choosing a treatment plan, the stage of the leukemia and other prognostic factors (see "How is chronic lymphocytic leukemia staged?") are important. Other factors to consider include whether or not you are having symptoms, your age and overall health, and the likely benefits and side effects of treatment.

In considering your treatment options it is often a good idea to seek a second opinion, if possible. This may provide you with more information and help you feel more confident about the treatment plan you have chosen.

Chemotherapy

Chemotherapy (chemo) is the use of anti-cancer drugs that are taken by mouth or injected into a vein into a muscle to destroy or control cancer cells. When given this way, these drugs enter the bloodstream and reach all areas of the body, making this treatment useful for cancers such as leukemia that spread throughout the body. When treating certain types of leukemia, chemo may also be injected into the cerebrospinal fluid. Chemo given into the CSF is often the best way to treat leukemia in the area around the brain and spinal cord. This type of chemo, called *intrathecal chemotherapy*, is rarely needed to treat chronic lymphocytic leukemia (CLL).

Doctors give chemotherapy in cycles, with each period of treatment followed by a rest period to allow the body time to recover. Chemotherapy cycles generally last about 3 to 4 weeks. Chemotherapy is often not recommended for patients in poor health, but advanced age by itself is not a barrier to getting chemotherapy.

The major types of chemotherapy drugs that are used to treat CLL include:

Purine analogs include fludarabine (Fludara[®]), pentostatin (Nipent[®]), and cladribine (2-CdA, Leustatin[®]). Fludarabine is often one of the first drugs used against CLL. These drugs can have major side effects, including an increased risk of infection.

Alkylating agents, which include chlorambucil (Leukeran[®]) and cyclophosphamide (Cytoxan[®]), have been around much longer. They are often used along with a purine analog or with other chemotherapy drugs. They may also be used by themselves (or along with a steroid drug), especially in people who can't tolerate more aggressive treatment.

A newer drug called bendamustine (Treanda[®]) is an alkylating agent that has some properties of a purine analog.

Corticosteroids such as prednisone, methylprednisolone, and dexamethasone.

Other drugs sometimes used for CLL include doxorubicin (Adriamycin[®]), methotrexate, oxaliplatin, vincristine (Oncovin[®]), etoposide (VP-16), and cytarabine (ara-C).

Possible side effects

Chemotherapy drugs work by attacking cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow, 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 side effects.

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

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Low blood counts

Chemo can affect bone marrow, leading to low blood cell counts. This can cause:

- Increased risk of infections (due to low white blood cell counts)
- Easy bruising or bleeding (due to low blood platelets)
- Fatigue (due to low red blood cells)

These side effects are usually short-term and go away once treatment is finished. There are often ways to lessen these side effects. For example, there are drugs to help prevent or reduce nausea and vomiting. Be sure to ask your doctor or nurse about medicines to help

reduce side effects, and let him or her know when you do have side effects so they can be managed effectively.

Drugs known as growth factors (G-CSF and GM-CSF, for example) are sometimes given to increase the white blood cell counts and thus reduce the chance of infection.

If your white blood counts are very low during treatment, you can reduce your risk of infection by carefully avoiding exposure to germs. During this time, your doctor may tell 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 when they come in contact with you.
- Avoid large crowds and people who are sick (wearing a surgical mask offers some protection in these situations).

Antibiotics may be given before there are signs of infection or at the earliest sign that an infection may be developing. Drugs that help prevent viral and fungal infections may also be given.

Because many of the side effects of chemotherapy are caused by low white blood cell counts, some people find it helpful to keep track of their counts. If you are interested in this, ask your doctor or nurse about your blood cell counts or other blood tests and what these numbers mean.

If platelet counts are low, you may be given drugs or platelet transfusions to help protect against bleeding. Shortness of breath and extreme fatigue caused by low red blood cell counts may be treated with drugs or with red blood cell transfusions.

Tumor lysis syndrome is another possible side effect of chemotherapy. It is most common in patients who had large numbers of leukemia cells in the body before treatment and occurs most often with the first cycle of chemo. When the cells are killed, they break open and release their contents into the bloodstream. This can overwhelm the kidneys, which cannot get rid of all of these substances at once. This can lead to build up of excess amounts of certain minerals in the blood and even kidney failure. The excess minerals can lead to problems with the heart and nervous system. Doctors work to prevent these problems by giving the patient extra fluids and certain drugs, such as sodium bicarbonate, allopurinol, and rasburicase.

Monoclonal antibodies

Monoclonal antibodies are man-made versions of immune system proteins (antibodies) that are designed to attach to a specific target (in this case, proteins on the surface of cancer cells). These drugs can help the patient's immune system react and destroy the cancer cells.

Rituximab

Rituximab (Rituxan) is a monoclonal antibody that targets the CD20 antigen, which is found on the surface of B lymphocytes. It is used mainly to treat certain kinds of non-Hodgkin lymphoma, but it has also become one of the main treatments for chronic lymphocytic leukemia (CLL). It is most often used along with chemotherapy, either as part of the initial treatment or as part of a second-line regimen, but it may also be used by itself.

Rituximab is given by injection into a vein (IV), usually once a week. It can also be given once a month or every few months. Common side effects are usually mild but may include chills, fever, nausea, rashes, fatigue, and headaches. Rarely, more severe side effects occur during infusions (while the drug is being given), such as trouble breathing and low blood pressure. Even if these symptoms occur during the first rituximab infusion, it is very unusual for them to recur with later doses. Rituximab can cause hepatitis B infections that were dormant (inactive) to become active again, sometimes leading to severe liver problems or even death. For that reason, your doctor may check your blood for signs of an old hepatitis infection before starting this drug. This drug may also increase a person's risk of certain infections for many months after the drug is stopped.

In rare cases of patients with very high white blood cell counts, the drug may cause a condition called *tumor lysis syndrome* (this was discussed in detail in the chemotherapy section). This happens when the drug kills the cancer cells so quickly that the body has trouble getting rid of the breakdown products of the dead cells. It generally only occurs during the first course of treatment.

Alemtuzumab

Alemtuzumab (Campath[®]) is a monoclonal antibody that targets the CD52 antigen, which is found on the surface of CLL cells and many T lymphocytes. It is used mainly in patients with CLL that is no longer responding to standard chemotherapy treatments, but it can be used earlier in the disease.. It may prove to be especially useful in cases of CLL with a chromosome 17 deletion, which are often resistant to standard treatments.

Alemtuzumab is given by injection into a vein (intravenous or IV), usually several times a week. In studies, it has also been given as an injection under the skin (subcutaneously), but giving it this way is not approved by the Food and Drug Administration. The most common side effects are fever, chills, nausea, and rashes during the injection, but these effects seem to be less of a problem when it is given under the skin. It can also cause very low white blood cell counts, which increases the risk for severe bacterial and viral infections. Antibiotic and antiviral medicines are given to help protect against some of these infections, but severe and even life-threatening infections can still occur. It may also cause low red blood cell and platelet counts.

Ofatumumab

Ofatumumab (Arzerra[®]) is another monoclonal antibody that targets the CD20 antigen. It is used mainly in patients with CLL that is no longer responding to other treatments such as chemotherapy or alemtuzumab.

Ofatumumab is given by injection into a vein (intravenous or IV) over several hours. The standard course is once a week for 8 weeks, followed by once a month for 4 months. Infusion reactions, including fever, chills, nausea, swelling, blood pressure changes, and rashes, are common during the infusion, so medicines are given beforehand to try to lower this risk. This drug can increase a person's risk of infections. Other side effects are less common but are potentially serious, including low platelet counts (with increased risk of bleeding) and blockage (obstruction) of the intestines.

Surgery

Surgery has a very limited role in the treatment of chronic lymphocytic leukemia (CLL). Because CLL cells spread so widely throughout the bone marrow and to many organs, surgery cannot cure this type of cancer. It rarely has any role even in the diagnosis of CLL, which can often be made with a blood sample. Minor surgery is sometimes needed to remove a lymph node to aid in diagnosing or staging the cancer.

Splenectomy

In rare cases, the spleen may be removed (splenectomy). This is not expected to cure the leukemia, but it can help improve some of the symptoms. Sometimes the spleen becomes so large that it presses on nearby organs and causes symptoms. If radiation or chemotherapy does not help shrink the spleen and reduce symptoms, splenectomy may be an option.

Splenectomy may also improve blood cell counts and lower the need for blood product transfusions. One of the spleen's normal functions is to remove worn-out blood cells from the bloodstream. If leukemia or other diseases cause the spleen to become too large, it may become too active in removing blood cells, leading to a shortage of red blood cells or platelets. Taking out the spleen may help prevent this. Splenectomy is used much more often for hairy cell leukemia than for regular CLL.

Most people have no problem living without a spleen. The risk for certain bacterial infections is increased, which is why doctors often recommend certain vaccines for people who have had their spleen removed.

Radiation therapy

Radiation therapy is treatment with high-energy rays or particles to destroy cancer cells. Radiation therapy is usually not part of the main treatment for people with chronic lymphocytic leukemia (CLL), but it is used in certain situations.

Patients may have symptoms if swollen internal organs (such as an enlarged spleen) press on other organs. For instance, pressure against the stomach may affect appetite. If these symptoms are not improved by chemotherapy, radiation therapy to help shrink the organ is often a good option.

Radiation therapy can also be useful in treating pain from bone damage caused by leukemia cells growing in the bone marrow.

Radiation therapy is sometimes given in low doses to the whole body, just before a stem cell transplant (see the section, "Bone marrow or peripheral blood stem cell transplant").

External beam radiation therapy, in which a machine delivers a beam of radiation to a specific part of the body, is the type of radiation used most often for CLL. Before your treatment starts, the radiation team will take careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. Radiation therapy is much like getting an x-ray, but the radiation is more intense. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time -- getting you into place for treatment -- usually takes longer.

The main short-term side effects of radiation therapy depend on where the radiation is aimed. Sunburn-like skin changes in the treated area are possible. Radiation to the abdomen can sometimes cause nausea, vomiting, or diarrhea. For radiation that includes large parts of the body, the effects may include fatigue and an increased risk of infection.

Bone marrow or peripheral blood stem cell transplant

The usual doses of chemotherapy drugs can cause serious side effects to quickly dividing tissues such as the bone marrow. Even though higher doses of these drugs might be more effective, they are not given because they could severely damage to bone marrow, which is where new blood cells are formed. This could lead to life-threatening infections, bleeding, and other problems because of low blood cell counts.

A stem cell transplant (SCT) allows doctors to use higher doses of chemotherapy and, sometimes, radiation therapy. After treatment is finished, the patient receives a transplant of blood-forming stem cells to restore the bone marrow.

Blood-forming stem cells used for a transplant are obtained either from the blood (for a peripheral blood stem cell transplant, or PBSCT) or from the bone marrow (for a bone marrow transplant, or BMT). Bone marrow transplant was more common in the past, but it has largely been replaced by PBSCT.

It's not yet clear how helpful stem cell transplants are in patients with chronic lymphocytic leukemia (CLL). When these treatments are used, it is most often in clinical trials looking to test their effectiveness.

Types of transplants

There are 2 main types of stem cell transplants: allogeneic and autologous. They differ in the source of the blood-forming stem cells.

Allogeneic stem cell transplant

In an allogeneic transplant, the stem cells come from someone else - usually a donor whose tissue type is almost identical to the patient's. Tissue type is based on certain substances on the surface of cells in the body. These substances can cause the immune system to react against the cells. Therefore, the closer a tissue match is between the donor and the recipient, the better the chance the transplanted cells will take and begin making new blood cells.

The donor may be a brother or sister if they are a good match. Less often, a matched unrelated donor may be found. The stem cells from an unrelated donor come from volunteers whose tissue type has been stored in a central registry and matched with that of the patient. Sometimes umbilical cord stem cells are used. These stem cells come from blood drained from the umbilical cord and placenta after a baby is born and the umbilical cord is cut.

Allogeneic transplants are being studied in patients with CLL, although it's not yet clear how effective they are. Because this type of transplant can cause severe or even life-threatening complications and side effects, it may not be a good option in people who are older or have other health problems.

Non-myeloablative transplant (mini-transplant): Many people over the age of 55 can't tolerate a standard allogeneic transplant that uses high doses of chemotherapy. Some may be able to have a non-myeloablative transplant (also known as a *mini-transplant* or *reduced-intensity* transplant), where they receive lower doses of chemotherapy and radiation that do not completely destroy the cells in their bone marrow. They then receive the allogeneic (donor) stem cells. These cells enter the body and establish a new immune system, which sees the leukemia cells as foreign and attacks them (a graft-versus-leukemia effect).

Doctors have learned that if they use small doses of certain chemotherapy drugs and low doses of total body radiation, an allogeneic transplant can still sometimes work with much less toxicity. In fact, a patient can receive a non-myeloablative transplant as an outpatient. The major complication is graft-versus-host disease.

Many doctors still consider this procedure to be experimental for CLL and feel it is best done as part of a clinical trial.

Autologous stem cell transplant

In an autologous transplant, a patient's own stem cells are removed from his or her bone marrow or peripheral blood. They are frozen and stored while the person gets treatment (high-dose chemotherapy and/or radiation). A process called *purging* may be used to try to remove any leukemia cells in the samples. The stem cells are then reinfused into the patient's blood after treatment.

Autologous transplants are generally easier for patients to tolerate than allogeneic transplants. The patient is getting his or her own cells back, so the risk of complications is smaller. This type of transplant can be done in any otherwise healthy person, but it might not be suitable for elderly patients.

Autologous stem cell transplants are being studied for use in CLL, but so far it isn't clear if they improve survival compared with standard treatment.

The transplant procedure

Blood-forming stem cells from the bone marrow or peripheral blood are collected, frozen, and stored. The patient receives high-dose chemotherapy and sometimes also radiation treatment to the entire body. (Radiation shields are used to protect the lungs, heart, and kidneys from damage during radiation therapy.)

The treatments are meant to destroy any cancer cells in the body. They also kill the normal cells of the bone marrow and the immune system. After these treatments, the frozen stem cells are thawed and given as a blood transfusion. The stem cells settle into the patient's bone marrow over the next several days and start to grow and make new blood cells.

In allogeneic SCTs, the person getting the transplant may be given drugs to keep the new immune system in check. For the next few weeks the patient gets regular blood tests and supportive therapies as needed, which might include antibiotics, red blood cell or platelet transfusions, other medicines, and help with nutrition.

Usually within a couple of weeks after the stem cells have been infused, they begin making new white blood cells. This is followed by new platelet production and, several weeks later, new red blood cell production.

Patients usually stay in the hospital in protective isolation (guarding against exposure to germs) until their white blood cell count rises above 500. They may be able to leave the hospital when their white blood cell count is near 1,000. Because platelet counts take longer to return to a safe level, patients may get platelet transfusions as outpatients.

Patients typically make regular visits to the outpatient clinic for about 6 months, after which their care is continued by their cancer doctor.

Practical points

Bone marrow or peripheral blood SCT is a complex treatment. If the doctors think a patient may benefit from a transplant, it should be done at a hospital where the staff has experience with the procedure and with managing the recovery phase. Some bone marrow transplant programs may not have experience in certain types of transplants, especially transplants from unrelated donors.

SCT is very expensive (more than \$100,000) and often requires a long hospital stay. Because some insurance companies may view it as an experimental treatment, they may not pay for the procedure. It is important to find out what your insurer will cover before deciding on a transplant to get an idea of what you might have to pay.

Possible side effects

Side effects from SCT are generally divided into early and long-term effects.

The early complications and side effects are basically the same as those caused by any other type of high-dose chemotherapy (see the "Chemotherapy" section of this document), and are caused by damage to the bone marrow and other quickly dividing tissues of the body. They can include low blood cell counts (with fatigue and increased risk of infection and bleeding), nausea, vomiting, loss of appetite, mouth sores, and hair loss.

One of the most common and serious short-term effects is the increased risk of infection from bacteria, viruses, or fungi. Antibiotics are often given to try to prevent this from happening. Other side effects, like low red blood cell and platelet counts, may require blood product transfusions or other treatments.

Some complications and side effects can persist for a long time or may not occur until months or years after the transplant. These include:

- Graft-versus-host disease (GVHD), which can occur in allogeneic (donor) transplants. This happens when the donor immune system cells attack tissues of the patient's skin, liver, and digestive tract. Symptoms can include weakness, fatigue, dry mouth, rashes, nausea, diarrhea, yellowing of the skin and eyes (jaundice), and muscle aches. In severe cases, GVHD can be life-threatening. GVHD is often described as either acute or chronic, based on how soon after the transplant it begins. Drugs that weaken the immune system are often given to try to keep GVHD under control.
- Radiation damage to the lungs, causing shortness of breath
- Damage to the ovaries in women, causing infertility and loss of menstrual periods
- Damage to the thyroid gland that causes problems with metabolism
- Cataracts (damage to the lens of the eye that can affect vision)
- Bone damage called aseptic necrosis (where the bone dies because of poor blood supply). If damage is severe, the patient will need to have part of the bone and the joint replaced.

For more information on stem cell transplants, see our document, *Bone Marrow and Peripheral Blood Stem Cell Transplant*.

Clinical trials

You may have had to make a lot of decisions since you've been told you have cancer. 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 your type of cancer. 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. 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.

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 cancer treatment. They are the only way for doctors to learn better methods to treat cancer. 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

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and Web sites 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 cancer. 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 cancer 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 the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with 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 cancer.

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 cancers? 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 cancer 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 chronic lymphocytic leukemia by risk group

Treatment options for people with chronic lymphocytic leukemia (CLL) vary greatly, depending on their age, the disease risk group, and the reason for treating (like the symptoms the leukemia is causing). While many people live a long time with CLL, in general it is very difficult to cure, and early treatment hasn't been shown to help people live longer. Because of this and because treatment can cause side effects, doctors often advise waiting until the disease is progressing or symptoms appear before starting treatment.

The risk group, based on the Rai staging system (see the section "How is chronic lymphocytic leukemia staged?"), is one factor when looking at treatment options. A person's age, general health, and other prognostic factors are important as well. Newer lab tests that look at chromosome changes and molecular markers may also offer important information about a patient's outlook. For example, people whose CLL cells have chromosome 17 deletions or high levels of ZAP-70 and CD38 are more likely to have faster growing forms of CLL and may need to be treated more aggressively. Tests for these changes are just starting to be included when looking at treatment options.

Low-risk CLL

People in this group are often diagnosed based on a high lymphocyte count in the blood but otherwise have normal blood counts and do not have enlarged lymph nodes or organs. The prognosis (outlook) for people in this group is often very good, with long survival expected.

Most people can be observed with careful and frequent follow-up exams. Treatment is considered if there are signs that the leukemia is progressing or if a person develops bothersome symptoms. When needed, initial treatment is usually chemotherapy, as described in the next section.

Intermediate- and high-risk CLL

Some patients with intermediate-risk CLL (stages I and II) may not have any symptoms and might not need treatment right away. They can often be watched for signs of disease progression and the start of new symptoms. Patients with high-risk CLL (stages III and IV) are more likely to need immediate treatment.

When treatment is needed there are several options. What treatment is used will depend upon factors such as the patient's health, possible side effects, the reason that treatment is needed, and any need for a rapid response. Commonly used treatments include:

- FCR: fludarabine (Fludara), cyclophosphamide (Cytosan), and rituximab (Rituxan)
- PCR: pentostatin (Nipent), cyclophosphamide, and rituximab
- FR: fludarabine and rituximab
- CVP: cyclophosphamide, vincristine, and prednisone (sometimes with rituximab)
- CHOP: cyclophosphamide, doxorubicin, vincristine (Oncovin), and prednisone
- Chlorambucil and prednisone
- Bendamustine
- Alemtuzumab (Campath)
- Fludarabine

Other drugs or combinations of drugs may also be used.

If the only problem is an enlarged spleen or swollen lymph nodes in one region of the body, localized treatment with low-dose radiation therapy may be used. Splenectomy (surgery to remove the spleen) is another option if the enlarged spleen is causing symptoms.

Some people who have very high-risk disease may be best treated early with some type of stem cell transplant (SCT). Because it's still not clear how effective this treatment is for CLL, most stem cell transplants are done as part of a clinical trial. Younger people

may be eligible for an autologous or allogeneic SCT. Some older people who may not be able to tolerate such transplants may still be eligible for a non-myeloablative transplant (mini-transplant).

Second-line treatment of CLL

If the initial treatment is no longer working or the disease comes back, another type of treatment may help. If the initial response to the treatment lasted a long time (usually at least a few years), the same treatment can often be used again. If the initial response wasn't long-lasting, using the same treatment again isn't as likely to be helpful. The options will depend on what the first-line treatment was and how well it worked, as well as the person's health.

Many of the drugs and combinations listed above may be options as second-line treatments. For many people who have already had fludarabine, alemtuzumab seems to be helpful as second-line treatment, although it carries an increased risk of infections. Other purine analog drugs, such as pentostatin or cladribine (2-CdA), may also be tried. Ofatumumab may be another option if other second-line treatments are no longer working.

Some people may have a good response to first-line treatment (such as fludarabine) but may still have some evidence of a small number of leukemia cells in the blood, bone marrow, or lymph nodes. This is known as *minimal residual disease*. Because CLL can't be cured, doctors aren't sure if further treatment right away will be helpful. Some small studies have shown that alemtuzumab can sometimes help get rid of these remaining cells, but it's not yet clear if this improves survival.

Treatment of complications of CLL

CLL can cause serious problems with the blood and some of its components. It can also (rarely) transform into another, more aggressive type of cancer. Treatment of CLL itself may also lead to the development of another cancer.

Sometimes very high numbers of leukemia cells in the blood cause problems with normal circulation. Chemotherapy may not lower the number of cells until a few days after the first dose. In the meantime, leukapheresis may be used before chemotherapy. For this procedure, a needle is placed into a vein in the arm. The patient's blood is passed through a special machine that removes white blood cells (including leukemia cells) and returns the rest of the blood cells and plasma to the patient. This treatment lowers blood counts right away. The effect is only for a short time, but it may help until the chemotherapy has a chance to work.

People with CLL often have weakened immune systems and are at high risk for certain kinds of infections. Doctors may suggest vaccines to prevent some of these infections. Finding and treating infections early is an important part of follow-up for people with CLL, even in those who aren't getting treatment with chemotherapy.

Sometimes CLL alters a patient's immune system in a way that causes it to attack his or her own red blood cells (called *auto-immune hemolytic anemia*) or blood platelets (*immune-mediated thrombocytopenia*). These conditions are treated with drugs that weaken the immune response. Steroids such as prednisone are often helpful, as are other drugs such as cyclosporine. Monoclonal antibodies like rituximab can also help in some cases.

One of the most serious complications of CLL is a change (transformation) of the leukemia to a high-grade or aggressive type of non-Hodgkin lymphoma called diffuse large cell lymphoma. This happens in about 5% of CLL cases, and is known as *Richter syndrome*. Treatment is often the same as it would be for lymphoma (see our document, *Non-Hodgkin Lymphoma* for more information), but these cases are often hard to treat.

Less often, CLL may transform to *prolymphocytic leukemia*. As with Richter syndrome, these cases can be hard to treat. Some studies have suggested that certain drugs such as cladribine (2-CdA) and alemtuzumab may be helpful.

In rare cases, patients with CLL may have their leukemia transform into acute lymphocytic leukemia (ALL). If this happens, treatment is likely to be similar to that used for patients with ALL (see our document, *Leukemia: Acute Lymphocytic*).

Acute myeloid leukemia (AML) is another rare complication in patients who have been treated for CLL. Drugs such as chlorambucil and cyclophosphamide can damage the DNA of blood-forming cells. These damaged cells may go on to become cancerous, leading to AML, which is very aggressive and often hard to treat (see our document, *Leukemia: Acute Myeloid*).

Treatment of hairy cell leukemia

Hairy cell leukemia (HCL) tends to be slow growing. Patients without symptoms often don't need to be treated right away, but they do need to have careful follow-up exams. These are done every few months to check for disease progression and appearance of symptoms. Some patients with HCL live for many years without having any symptoms or receiving any treatment.

Treatment may be advised for HCL patients with low blood cell counts, recurrent infections, or an enlarged spleen or lymph nodes. Treatment is most often with one of the purine analog drugs -- either cladribine (2-CdA) or pentostatin. Up to 80% to 90% of patients respond to these drugs, and the responses last more than 5 years in most patients. Even if HCL recurs, many cases will respond to a second treatment with these drugs.

Giving rituximab after these drugs may get rid of any remaining disease in people who haven't fully responded. Because this is a fairly rare disease, too few people have been treated with rituximab to know if it will make a long-term difference.

In rare cases, HCL may not respond to chemotherapy. Rituximab or interferon-alfa, a type of biologic therapy, may be helpful. If a patient is uncomfortable because of an enlarged spleen, removing the spleen by surgery (splenectomy) can often help relieve pain or other symptoms.

More treatment information

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN Web site (www.nccn.org). Treatment guidelines for chronic lymphocytic leukemia (CLL) are included in the Non-Hodgkin's Lymphomas guidelines (because CLL is closely related to some forms of lymphoma).

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What should you ask your doctor about chronic lymphocytic leukemia?

As you cope with cancer and cancer treatment, you need to have honest, open discussions with your doctor. You should 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. Nurses, social workers, and other members of the treatment team may also be able to answer many of your questions.

- What is the stage (risk group) of the leukemia, and what does that mean in my case?
- Are there other tests that need to be done before we can decide on treatment?
- How much experience do you have treating this type of cancer?
- Should I get a second opinion?
- Should I be treated at this time? Why or why not?
- What treatment choices do I have?
- What do you recommend, and why?
- What are the risks and side effects with the treatments that you recommend?
- 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 the outlook for my survival?
- What would we do if the treatment doesn't work or if the leukemia recurs?

- What type of follow-up will I need after treatment?

Be sure to write down any questions that occur to you that are not on this list. For instance, you might want information about recovery times so that you can plan your work schedule. Or you may want to ask about clinical trials for which you may qualify.

Taking another person and/or a tape recorder to your doctor visit can be helpful. Collecting copies of your medical records, pathology reports, and radiology reports may be useful in case you wish to seek a second opinion at a later time.

What happens after treatment for chronic lymphocytic leukemia?

Chronic lymphocytic leukemia (CLL) is rarely able to be cured. Still, most patients live for many years with the disease. Some CLL patients can live for years without treatment, but most eventually need to be treated. Most patients with CLL are treated on and off for years. Treatment may stop for a while, but it never really ends. Learning to live with cancer that does not go away can be difficult and very stressful.

Follow-up care

Before, during, and after treatment, your doctors will 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 may have and may do exams and 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. This 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. It is important that you report any new symptoms to the doctor right away so that the cause can be found and treated, if needed.

Checkups may include careful physical exams, blood tests, and other tests as needed. A benefit of follow-up care is that it gives you a chance to discuss questions and concerns that can arise.

Treatment of CLL is not expected to cure the disease. This means that even if there are no signs of leukemia after treatment (known as a complete remission), the leukemia is likely to come back again (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. For more information on how recurrent CLL is treated, see the section "How is chronic lymphocytic leukemia treated?" For more general information on dealing with a recurrence, you may also want to see our document, *When Your Cancer Comes Back: Cancer Recurrence*. You can get this document by calling 1-800-227-2345.

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.

Most people with CLL do not have normally functioning immune systems, which may raise their risk for certain infections. Some treatments for CLL, such as alemtuzumab and many chemotherapy drugs, may also raise this risk. Your doctor may recommend vaccines or other medicines to help prevent or control certain infections.

People with CLL are also at increased risk of developing a second cancer. At least some of this increased risk may be due to the effects of CLL on the immune system.

Treatments for CLL may also raise the risk of some cancers. The most common second cancers in people with CLL are skin and lung cancers, although other types of leukemia, lymphoma, and other blood cancers are also possible. It is important to be aware of this increased risk and to report any possible symptoms to your doctor right away.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know anything about your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. 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 were in the hospital, a copy of the discharge summary that doctors prepare when patients are sent home
- If you had radiation therapy, a copy of the treatment summary
- If you had chemotherapy or other medicines, a list of your drugs, drug doses, and when you took them

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

Lifestyle changes

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. This 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. Try to eat 5 or more servings of vegetables and fruits each day. Choose whole grain foods instead of those made with white flour and sugars. Try to limit meats that are high in fat. Cut back on processed meats like hot dogs, bologna, and bacon. Better yet, don't eat any of these, if you can. If you drink alcohol, limit yourself to 1 or 2 drinks a day at the most.

Rest, fatigue, work, 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 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. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis twice a week. If you haven't exercised 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 exercise 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 our documents *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 makes you feel happier.
- It helps you feel better about yourself.

And long term, we know that exercise plays a role in helping to lower the risk of some cancers. In the American Cancer Society guidelines on physical activity for cancer prevention, we recommend that adults take part in at least 30 minutes of moderate to vigorous physical activity, above usual activities, on 5 or more days of the week; 45 to 60 minutes of intentional physical activity are even better.

How about your emotional health?

When treatment is over (even for a while), 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.

If treatment stops working

When chronic lymphocytic leukemia (CLL) keeps growing or comes back after one treatment, another treatment plan is likely to help, at least for a while. 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 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.

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 about hospice in our document called *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 chronic lymphocytic leukemia research and treatment?

There are many studies of chronic lymphocytic leukemia (CLL) being done in labs and in clinical trials around the world.

Genetics of chronic lymphocytic leukemia

Scientists are making great progress in understanding how changes in a person's DNA can cause normal bone marrow cells to develop into leukemia cells. Learning about changes in the genes (regions of the DNA) that often occur in CLL is providing insight into why these cells grow too quickly, live too long, and fail to develop into normal blood cells. Doctors are also learning how to use these changes to help them determine a person's outlook and whether they will need treatment.

In recent years, researchers have found that CLL can be divided into 2 broad groups, based on whether or not there are mutations in the VH gene. The status of this gene gives some information about how mature the leukemia cells are, and how quickly the leukemia is likely to grow. Cells that have changes in the VH gene are more mature, and people with this form of CLL seem to have a better outlook than those without these changes. This might be important when deciding if people need treatment. Tests for VH gene changes are not yet widely available, but they may be within the next few years. In the meantime, tests for ZAP-70 and CD38 seem to provide similar -- if not exactly the same -- information with regard to outlook.

New treatment combinations

Many different drugs are now used to treat CLL. Doctors are looking into which combinations of these drugs are most effective, offering the best chance for long-term survival with the fewest side effects.

The role of stem cell transplants in CLL is still not well-defined. Doctors aren't sure which type of transplant (autologous, allogeneic, or mini-transplant) might be most effective, or which drugs should be used along with the transplant. Studies are now being done to try to answer these questions.

New drugs for chronic lymphocytic leukemia

Dozens of new drugs are being tested for use against CLL. Many of these drugs are targeted at specific parts of cancer cells, while others are more like standard chemotherapy drugs. Flavopiridol and lenalidomide are 2 drugs that have shown promise in early studies against some hard-to-treat cases of CLL.

Oblimersen (Genasense[®]) is a drug that has been studied for use in CLL. In studies, giving this drug along with chemo was more likely than chemo alone to cause the CLL to go into remission and stay there.

A number of new monoclonal antibodies (man-made versions of immune system proteins) are now being studied for use in CLL treatment. Some of these antibodies, such as lumiliximab and ofatumumab, are used to try to prompt the immune system to attack leukemia cells. They are being tested either alone or in combination with chemotherapy.

Other antibodies are attached to substances that can poison cancer cells, and are known as immunotoxins. They act as homing devices to deliver the toxins directly to the cancer cells. An immunotoxin known as BL22 has shown a great deal of promise in treating hairy cell leukemia (HCL) in clinical trials. A newer version of this drug, known as HA22 (CAT-8015) is now being tested for use against CLL.

Additional resources

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.

After Diagnosis: A Guide for Patients and Families (also available in Spanish)

Bone Marrow and Peripheral Blood Stem Cell Transplant

Caring for the Patient With Cancer at Home (also available in Spanish)

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

When Your Cancer Comes Back: Cancer Recurrence

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's Guide to Pain Control

Cancer in the Family: Helping Children Cope With a Parent's Illness

Caregiving: A Step-By-Step Resource for Caring for the Person With Cancer at Home

When the Focus Is on Care: Palliative Care and Cancer

National organizations and Web sites*

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

Chronic lymphocytic leukemia

Leukemia & Lymphoma Society

Toll-free number: 1-800-955-4572

Web site: www.lls.org

National Cancer Institute

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

Web site: www.cancer.gov

Bone marrow and peripheral blood stem cell transplants

Caitlin Raymond International Registry (for unrelated bone marrow transplants)

Toll-free number: 1-800-726-2824

Web site: www.crir.org

National Bone Marrow Transplant Link (nbmtLINK)

Toll-free number: 1-800-LINK-BMT (1-800-546-5268)

Web site: www.nbmtlink.org

National Marrow Donor Program

Toll-free number: 1-800-MARROW-2 (1-800-627-7692)

Web site: www.marrow.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.

References

Altekruse SF, Kosary CL, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2007, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2007/, based on November 2009 SEER data submission, posted to the SEER web site, 2010.

American Cancer Society. *Cancer Facts and Figures 2010*. Atlanta, Ga: American Cancer Society; 2010.

Grever MR, Andritsos LA, Lozanski G. Chronic lymphoid leukemias. In: Abeloff MD, Armitage JO, Niederhuber JE, Kastan MB, McKenna WG, eds. *Abeloff's Clinical Oncology*. 4th ed. Philadelphia, Pa: Elsevier; 2008:2293–2308.

Gribben JG. Molecular profiling in CLL. In: *Hematology 2008*. American Society of Hematology Education Program Book. 2008:444-449. Accessed at <http://asheducationbook.hematologylibrary.org/cgi/content/full/2008/1/444> on March 31, 2009.

National Cancer Institute. Physician Data Query (PDQ). Chronic Lymphocytic Leukemia Treatment. 7/8/2010. Accessed at www.cancer.gov/cancertopics/pdq/treatment/CLL/healthprofessional on September 28, 2010.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Non-Hodgkin's Lymphomas. V.1.2010. Accessed at www.nccn.org on September 24, 2010.

O'Brien S. New agents in the treatment of CLL. In: *Hematology 2008*. American Society of Hematology Education Program Book. 2008:457-464. Accessed at <http://asheducationbook.hematologylibrary.org/cgi/content/full/2008/1/457> on March 31, 2009.

O'Brien S, Moore JO, Boyd TE, et al. 5-year survival in patients with relapsed or refractory chronic lymphocytic leukemia in a randomized, phase III trial of fludarabine plus cyclophosphamide with or without oblimersen. *J Clin Oncol*. 2009 Nov 1;27(31):5208-12. Epub 2009 Sep 8.

Wierda WG, Keating MJ, O'Brien S. Chronic lymphoid leukemias. In: DeVita VT, Lawrence TS, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 8th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2008:2278–2292.

Wierda WG, Lamanna N, Weiss MA. Chronic lymphocytic leukemia. In: Pazdur R, Wagman LD, Camphausen KA, Hoskins WJ, eds. *Cancer Management: A Multidisciplinary Approach*. 11th ed. Lawrence, KS: CMPMedica; 2008:843–858.

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