LEUKEMIA--CHRONIC LYMPHOCYTIC

What is cancer?

Cancer develops when cells in a part of the body begin to grow out of control. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries.

Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells.

Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. Many times though, a person’s DNA becomes damaged by exposure to something in the environment, like smoking.

Cancer usually forms as a tumor. Some cancers, like leukemia, do not form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Often, cancer cells travel to other parts of the body, where they begin to grow and replace normal tissue. This process is called metastasis. Regardless of where a cancer may spread, however, it is always named for the place it began. For instance, breast cancer that spreads to the liver is still called breast cancer, not liver cancer.

Not all tumors are cancerous. Benign (non-cancerous) tumors do not spread (metastasize) to other parts of the body and, with very rare exceptions, are not life threatening.

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.

Cancer is the second leading cause of death in the United States. Nearly half of all men and a little over one third of all women in the United States will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking and eating a better diet. The sooner a cancer is found and treatment begins, the better are the chances for living for many years.

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 learned that there are probably 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 new lab tests can tell the difference between them. The tests look for a protein called ZAP-70 and for a substance called CD38. Patients whose CLL cells contain low amounts of ZAP-70 and CD38 have a better prognosis (outlook for survival).

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

In order to understand the different types of leukemia, it is helpful to have some basic knowledge 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.

The blood-forming cells come from blood *stem cells*. These stem cells only make new blood-forming cells and not other kinds of cells. (This makes them different from embryonic stem cells, which are formed in a developing fetus and can develop into most other cells in the body.)

Stem cells go through a series of changes. 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 weakness, fatigue, and shortness 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 are important in defending the body against 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 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 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 antibodies. These antibodies attach to the germs, such as bacteria, viruses, and fungi. Once the germ has been coated in this way, other white blood cells called granulocytes can recognize and destroy it. 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 are white blood cells that have granules in them, which are spots that can be seen under the microscope. These granules 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, 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 are also important in helping lymphocytes to 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. Although leukemia cells may reproduce quickly, in most cases the problem is that they don’t die when they should. They survive and accumulate. 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 can help doctors better predict each patient's prognosis (outlook) select the best treatment.

Acute Leukemia Versus Chronic Leukemia

The first factor to consider in classifying a patient's leukemia is if 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 are not really normal. They generally do not fight infection as well as do normal white blood cells. And, of course, 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. However, chronic leukemias are generally harder to cure than acute leukemias.

Myeloid Leukemia Versus Lymphocytic Leukemia

The second factor to consider 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* leukemia). Lymphomas are also cancers of lymphocytes. But, unlike lymphocytic leukemias, which develop in the bone marrow, lymphomas develop from lymphocytes in lymph nodes or other organs.

By considering whether they are acute or chronic, and whether they are myeloid or lymphocytic, leukemias 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 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): A rare 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

relapse. B-PLL may develop in someone who already has CLL (in which case it tends to be more aggressive). Or PLL can occur in people who have never had CLL.

Large granular lymphocyte (LGL) leukemia: 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, although aggressive cases are very hard to treat.

Hairy cell leukemia (HCL): A 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 the separate American Cancer Society documents on these topics.

What Are the Key Statistics About Chronic Lymphocytic Leukemia?

The American Cancer Society estimates that 15,110 new cases of chronic lymphocytic leukemia (CLL) will be diagnosed in the United States during 2008. About 4,390 people in the United States will die of CLL during 2008.

Chronic lymphocytic leukemia accounts for almost 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 are rarely absolute. 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.

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, although 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 maintain 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?

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 chronic lymphocytic leukemia (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 are blood cells from someone else with a different blood type. Scientists think that CLL begins because the B lymphocytes continue to divide without restraint after they have reacted to an antigen. 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 these inherited mutations very 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?

Although many types of cancer can be prevented by lifestyle changes to avoid certain risk factors, there are very few known risk factors for chronic lymphocytic leukemia (CLL). 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 can sometimes be 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?

Signs and Symptoms of Chronic Lymphocytic Leukemia

Many people with chronic lymphocytic leukemia (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. Even when there are symptoms, they are often vague and non-specific.

Symptoms of CLL can include the following:

- weakness
- fatigue
- 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

But these symptoms aren't found only in CLL. They can also occur with other cancers, as well as many non-cancerous conditions.

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 due to 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 are at higher risk for 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 hemolytic anemia (if the antibodies attack red blood cells), thrombocytopenia (if they attack the cells that make platelets), or leukopenia (if they attack white blood cells).

CLL often causes the liver or spleen to become enlarged. If these organs are enlarged, you may notice fullness or swelling of the belly. 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.

Types of Samples Used to Test for Chronic Lymphocytic Leukemia

If signs and symptoms 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 in order to 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 -- two tests that are usually done at the same time. The samples are usually taken from the back of the pelvic (hip) bone, although in some cases 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 area, the skin over the hip and the surface of the bone are numbed 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 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.

Excisional Lymph Node Biopsy

In this procedure, a surgeon cuts through the skin to remove an entire lymph node. 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 used 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.

Lumbar Puncture (Spinal Tap)

This procedure is used to look for leukemia cells in the cerebrospinal fluid (CSF), which 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 near the spine. A small 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 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 used to diagnose CLL or to help determine how advanced the disease is.

Blood Cell Counts and Blood Cell Exam

These tests look at the numbers of lymphocytes in the blood and at how they look under the microscope. Patients with CLL have too many of these white blood cells (lymphocytosis). More than 10,000 lymphocytes/mm³ (per cubic millimeter) of blood (normal is less than 5,000) 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.

Other Blood Tests

Other tests 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.

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-macroglobulin may be measured. High levels of this protein indicate a more advanced CLL.

Routine Microscopic Exam

Any samples taken (blood, bone marrow, lymph node tissue, or CSF) are looked at under a microscope by a pathologist (a doctor specializing in diagnosing diseases with lab tests) and may be reviewed by the patient's hematologist/oncologist (a doctor specializing in treating 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 circulating blood cells that can fight infections). Some leukemic cells can lack features of normal blood cells and are not effective in fighting infections. The most immature cells are called lymphoblasts (or "blasts" for short). Chronic lymphocytic leukemia cells usually appear mature.

An important 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

Cytochemistry tests involve exposing cells 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. These substances seem to be linked to what type of B lymphocyte is involved in the leukemia. Some recent studies suggest that CLL with fewer cells that express 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 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. The color change can be seen only by using a microscope.

Cytogenetics

This test involves looking at chromosomes (pieces of DNA) 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): A type of cytogenetic test that 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 and is very accurate, 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 commonly seen deletions involve parts of chromosomes 13, 11, or 17. 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 produce pictures of the inside of the body. There are several imaging tests that might be done in people with CLL. They are not needed to diagnose the leukemia, but they may be done to help determine the extent of the disease.

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.

Often after the first set of pictures is taken, you will receive an intravenous (IV) injection of a contrast dye or you may also be asked to drink a solution of contrast material. This helps to better outline blood vessels and internal organs. A second set of pictures is then taken.

The IV 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.

Magnetic Resonance Imaging (MRI) Scan

MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a very detailed image of parts of the body. Not only does this create images of cross-sectional slices of the body like a CT scanner, it can also produce images of slices that are parallel with the length of your body. A contrast material might be injected, just as with CT scans, but is used less often.

MRI scans are very helpful in looking at the brain and spinal cord.

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 upset people with a fear of enclosed spaces. Newer, "open" MRI machines can help with this if needed. The MRI machine makes loud buzzing noises that you may find disturbing. Some places provide headphones to block this out.

Ultrasound

Ultrasound uses sound waves and their echoes to produce a picture of internal organs or masses. For this test, a small, microphone-like instrument called a transducer is placed on the skin (which is first lubricated with oil). 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 that is displayed on a computer screen.

Ultrasound can be used 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. Most types of cancer are given stages of I, II, III, or IV, based on the size of the tumor and how far from the original site in the body the cancer has spread. Stages are useful because they guide your treatment. They also help determine your prognosis (outlook).

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 liver, spleen, 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

There are 2 different systems for staging CLL:

- Rai system -- used more often in the United States
- Binet system -- 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:** Lymphocytosis is present (the blood lymphocyte count is too high, usually defined as over 10,000 lymphocytes/mm^3 of blood. Some doctors will diagnose CLL if the count is over 5,000/mm^3 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.

The Rai stages can be separated into low-, intermediate-, and high-risk groups, which are often used to assess outlook and treatment options. Stage 0 is considered low risk, stages I and II are considered intermediate risk, and stages III and IV are considered high risk.

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 the presence of 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 useful 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 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, are still fairly new but can provide important information. These tests will likely 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.

Chemotherapy

Chemotherapy is the use of anti-cancer drugs that are injected into a vein or into the cerebrospinal fluid (CSF) or are taken by mouth to destroy or control cancer cells. Except when given into the CSF, 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.

Drugs called purine analogs, which include fludarabine (Fludara), pentostatin (Nipent), and cladribine (2-CdA, Leustatin), may be used against CLL. Fludarabine seems to be the most effective single drug, and it is often the first drug used against CLL. These drugs can have major side effects, including an increased risk of infection.

Drugs called 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.

Other drugs sometimes used for CLL include doxorubicin, vincristine, and prednisone.

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.

Chemotherapy Side Effects

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

- hair loss
- mouth sores
- loss of appetite

- nausea and vomiting
- lowered resistance to infection (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.

Be sure to talk with your cancer care team about any side effects you have because there are often ways to lessen them. For example, drugs can be given to prevent or reduce nausea and vomiting.

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 advise that you:

- 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. The most commonly used drugs are a combination of trimethoprim and sulfamethoxazole (Bactrim or Septra), which help fight bacteria. 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, don't hesitate to 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. Likewise, shortness of breath and extreme fatigue caused by low red blood cell counts may be treated with drugs or with red blood cell transfusions.

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, substances on the surface of cancer cells). This can help the patient's immune system react and destroy the cancer cells.

Alemtuzumab (Campath)

Alemtuzumab is a monoclonal antibody that targets the CD52 antigen, which is found on the surface of B and T lymphocytes. It is used mainly in patients with CLL that is no longer responding to standard chemotherapy treatments. Some studies are now testing its use earlier in the course of 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 either under the skin (subcutaneous) or into a vein (intravenous or IV), usually several times a week. The most common side effects are fever, chills, nausea, and rashes during the injection, although these effects seem to be less of a problem when it is given under the skin. It can also cause low white blood cell counts, which can increase the risk for bacterial and viral infections, so it is often given with antibiotic and antiviral medicines. It may also cause low red blood cell and platelet counts.

Rituximab (Rituxan)

Rituximab is a monoclonal antibody that targets the CD20 antigen, which is found on the surface of B lymphocytes. It is approved for use against certain kinds of non-Hodgkin lymphoma, but it has also been found to be useful in treating patients with CLL. It is most often used along with chemotherapy, either as part of the initial treatment or as part of a second-line regimen.

Rituximab is given by injection into a vein (IV), usually once a week. Other than the risk of fever when it is given, this drug has few side effects. In rare cases of patients with very high white blood cell counts, the drug may cause a condition called *tumor lysis syndrome*. The drug kills the cancer cells so quickly that the body has trouble getting rid of the breakdown products of the dead cells. These substances can build up and cause kidney problems. Medicines may be given to help prevent this.

Surgery

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

Splenectomy

Splenectomy (removal of the spleen) is rarely done, and is not expected to cure CLL. Spread of CLL to the spleen can cause that organ to become large enough to compress nearby organs and cause 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.

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 patients with 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 spleen 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").

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. 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 the severe damage to bone marrow cells would cause lethal shortages of blood cells and damage to vital organs.

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 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 with regard to the source of the blood-forming stem cells.

In an *allogeneic stem cell 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 present 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 or, less often, a matched unrelated donor (MUD). 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.

This type of transplant is being studied in patients with CLL, although it's not yet clear how effective it is. 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.

In an *autologous stem cell transplant,* a patient's own stem cells are removed from his or her bone marrow or peripheral blood. They are 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.

Autologous transplants are generally easier to tolerate than allogeneic transplants, as the patient is getting his or her own cells back. This type of transplant can be done in any otherwise healthy person, although very old patients might not be suitable.

Autologous stem cell transplants are being studied for use in chronic lymphocytic leukemia, 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 chemotherapy and radiation treatments are meant to destroy any remaining cancer cells. They also kill the normal cells of the bone marrow and the immune system. This prevents the stem cell transplant (graft) from being rejected. 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 is given drugs such as prednisone and methotrexate or cyclosporine to keep the immune system in check and prevent the body from rejecting the transplant. 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 receive platelet transfusions as an outpatient.

Patients typically make regular visits to the outpatient clinic for about 6 months, after which their care is continued by their cancer doctor. At this point, they only come back to the bone marrow transplant clinic for their annual exam, or if they have symptoms that should be brought to their doctor's attention.

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 lengthy hospital stay. Because some insurance companies 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 and to have an idea of what you might have to pay.

Transplant 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 due to damage to the bone marrow and other quickly dividing tissues of the body. They can include low blood cell counts (with 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 for 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 fatal. 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* (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.

Non-myeloablative Transplant (Mini-transplant)

Most patients 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 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.

This procedure is still considered experimental, and studies are under way to determine how useful it may be against CLL.

For more information on stem cell transplants, see the American Cancer Society document, *Bone Marrow and Peripheral Blood Stem Cell Transplants*.

Clinical Trials

You 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 deciding 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 one way to get state-of-the art cancer care. Still, they are not right for everyone.

Here we will give you a brief review of clinical trials. Talking to your health care team, your family, and your friends can help you make the best treatment choice for you.

What Are Clinical Trials?

Clinical trials are carefully controlled research studies that are done with patients. These studies test whether a new treatment is safe and how well it works in patients, or they may test new ways to diagnose or prevent a disease. Clinical trials have led to many advances in cancer prevention, diagnosis, and treatment.

The Purpose of Clinical Trials

Clinical trials are done to get a closer look at promising new treatments or procedures in patients. A clinical trial is only done when there is good reason to believe that the treatment, test, or procedure being studied may be better than the one used now. Treatments used in clinical trials are often found to have real benefits and may go on to become tomorrow's standard treatment.

Clinical trials can focus on many things, such as:

- new uses of drugs that are already approved by the US Food and Drug Administration (FDA)
- new drugs that have not yet been approved by the FDA
- non-drug treatments (such as radiation therapy)
- medical procedures (such as types of surgery)
- herbs and vitamins
- tools to improve the ways medicines or diagnostic tests are used
- medicines or procedures to relieve symptoms or improve comfort
- combinations of treatments and procedures

Researchers conduct studies of new treatments to try to answer the following questions:

- Is the treatment helpful?
- What's the best way to give it?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Are there more or fewer side effects than the standard treatment used now?
- Do the benefits outweigh the side effects?
- In which patients is the treatment most likely to be helpful?

Phases of Clinical Trials

There are 4 phases of clinical trials, which are numbered I, II, III, and IV. We will use the example of testing a new cancer treatment drug to look at what each phase is like.

Phase I clinical trials: The purpose of a phase I study is to find the best way to give a new treatment safely to patients. The cancer care team closely watches patients for any harmful side effects.

For phase I studies, the drug has already been tested in lab and animal studies, but the side effects in patients are not fully known. Doctors start by giving very low doses of the drug to

the first patients and increase the doses for later groups of patients until side effects appear or the desired effect is seen. Doctors are hoping to help patients, but the main purpose of a phase I trial is to test the safety of the drug.

Phase I clinical trials are often done in small groups of people with different cancers that have not responded to standard treatment, or that keep coming back (recurring) after treatment. If a drug is found to be reasonably safe in phase I studies, it can be tested in a phase II clinical trial.

Phase II clinical trials: These studies are designed to see if the drug works. Patients are given the best dose as determined from phase I studies. They are closely watched for an effect on the cancer. The cancer care team also looks for side effects.

Phase II trials are often done in larger groups of patients with a specific cancer type that has not responded to standard treatment. If a drug is found to be effective in phase II studies, it can be tested in a phase III clinical trial.

Phase III clinical trials: Phase III studies involve large numbers of patients -- most often those who have just been diagnosed with a specific type of cancer. Phase III clinical trials may enroll thousands of patients.

Often, these studies are randomized. This means that patients are randomly put in one of two (or more) groups. One group (called the control group) gets the standard, most accepted treatment. Another group (or more than one group) will get the new treatment being studied. All patients in phase III studies are closely watched. The study will be stopped early if the side effects of the new treatment are too severe or if one group has much better results than the others.

Phase III clinical trials are usually needed before the FDA will approve a treatment for use by the general public.

Phase IV clinical trials: Once a drug has been approved by the FDA and is available for all patients, it is still studied in other clinical trials (sometimes referred to as phase IV studies). This way more can be learned about short-term and long-term side effects and safety as the drug is used in larger numbers of patients with many types of diseases. Doctors can also learn more about how well the drug works, and if it might be helpful when used in other ways (such as in combination with other treatments).

What It Will Be Like to Be in a Clinical Trial

If you are in a clinical trial, you will have a team of experts taking care of you and watching your progress very carefully. Depending on the phase of the clinical trial, you may receive more attention (such as having more doctor visits and lab tests) than you would if you were

treated outside of a clinical trial. Clinical trials are specially designed to pay close attention to you.

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to find out. While most side effects go away in time, some may be long-lasting or even life threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide to enter (enroll in) a clinical trial.

Deciding to Enter a Clinical Trial

If you would like to take part in a clinical trial, you should begin by asking your doctor if your clinic or hospital conducts clinical trials. There are requirements you must meet to take part in any clinical trial. But whether or not you enter (enroll in) a clinical trial is completely up to you.

Your doctors and nurses will explain the study to you in detail. They will go over the possible risks and benefits and give you a form to read and sign. The form says that you understand the clinical trial and want to take part in it. This process is known as giving your informed consent. Even after reading and signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason.

Taking part in a clinical trial does not keep you from getting any other medical care you may need.

To find out more about clinical trials, talk to your cancer care team. Here are some questions you might ask:

- Is there a clinical trial that I could take part in?
- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do? Has it been used before?
- Will I know which treatment I receive?
- What is likely to happen in my case with, or without, this new treatment?
- What are my other choices and their pros and cons?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to stay in the hospital? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

How Can I Find Out More About Clinical Trials That Might Be Right for Me?

The American Cancer Society offers a clinical trials matching service for patients, their family, and friends. You can reach this service at 1-800-303-5691 or on our Web site at http://clinicaltrials.cancer.org.

Based on the information you give about your cancer type, stage, and previous treatments, this service can put together a list of clinical trials that match your medical needs. The service will also ask where you live and whether you are willing to travel so that it can look for a treatment center that you can get to.

You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

For even more information on clinical trials, the American Cancer Society has a document called *Clinical Trials: What You Need to Know.* You can read this on the Web site, www.cancer.org, or have it sent to you by calling 1-800-ACS-2345.

Complementary and Alternative Treatments

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that are different from mainstream (standard) medical treatment. These treatments can include vitamins, herbs, and special diets, or acupuncture and massage -- among many others. You may have a lot of questions about these treatments. Here are some you may have thought of already:

- How do I know if the treatment is safe?
- How do I know if it works?
- Should I try one or more of these treatments?
- What does my doctor know/think about these treatments? Should I tell the doctor that I'm thinking about trying them?
- Will these treatments cause a problem with my standard medical treatment?
- What is the difference between "complementary" and "alternative" treatments?
- Where can I find out more about these treatments?

The Terms Can Be Confusing

Not everyone uses these terms the same way, so it can be confusing. The American Cancer Society uses *complementary* to refer to medicines or treatments that are used *along with* your regular medical care. *Alternative* medicine is a treatment used *instead of* standard medical treatment.

Complementary treatments: Complementary treatment methods, for the most part, are not presented as cures for cancer. Most often they are used to help you feel better. Some methods that can be used in a complementary way are meditation to reduce stress, acupuncture to relieve pain, or peppermint tea to relieve nausea. There are many others. Some of these methods are known to help and could add to your comfort and well being, while others have not been tested. Some have been proven not to be helpful. A few have even been found harmful.

There are many complementary methods that you can safely use right along with your medical treatment to help relieve symptoms or side effects, to ease pain, and to help you enjoy life more. For example, some people find methods such as aromatherapy, massage therapy, meditation, or yoga to be useful.

Alternative treatments: Alternative treatments are those that are used instead of standard medical care. These treatments have not been proven to be safe and effective in clinical trials. Some of these treatments may even be dangerous or have life-threatening side effects. The biggest danger in most cases is that you may lose the chance to benefit from standard treatment. Delays or interruptions in your standard medical treatment may give the cancer more time to grow.

Deciding What to Do

It is easy to see why people with cancer may consider alternative treatments. You want to do all you can to fight the cancer. Sometimes mainstream treatments such as chemotherapy can be hard to take, or they may no longer be working.

Sometimes people suggest that their treatment can cure your cancer without having serious side effects, and it's normal to want to believe them. But the truth is that most non-standard treatments have not been tested and proven to be effective for treating cancer.

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

- Talk to your doctor or nurse about any treatment you are thinking about using.
- Check the list of "red flags" below.
- Contact the American Cancer Society at 1-800-ACS-2345 to learn more about complementary and alternative treatments in general and to learn more about the specific treatments you are thinking about.

Red Flags

You can use the questions below to spot treatments or methods to avoid. A "yes" answer to any one of these questions should raise a "red flag."

- Does the treatment promise a cure for all or most cancers?
- Are you told not to use standard medical treatment?
- Is the treatment or drug a "secret" that only certain people can give?
- Does the treatment require you to travel to another country?
- Do the promoters attack the medical or scientific community?

The Decision Is Yours

Decisions about how to treat or manage your cancer are always yours to make. If you are thinking about using a complementary or alternative method, be sure to learn about it and talk to your doctor about it. With reliable information and the support of your health care team, you may be able to safely use 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 CLL vary greatly, depending on the disease stage (risk group) and if the leukemia is causing any symptoms. Because CLL generally can't be cured 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) is one factor when looking at treatment options. Newer tests that look at chromosome changes and molecular markers (such as ZAP-70 and CD38) also offer important information about a patient's outlook. These tests are just starting to be included when looking at treatment options.

Low-risk CLL

The prognosis (outlook) for this group is often very good, with long survival expected. Most patients can be observed with careful and frequent follow-up exams. Treatment should be considered if there are signs that the leukemia is progressing or if the patient develops bothersome symptoms. When needed, initial treatment is usually chemotherapy, as described in the next section.

Intermediate- and High-risk CLL

Patients with intermediate- and high-risk CLL who do not have any symptoms may not need treatment right away. They can often be observed for signs of progression and onset of new symptoms.

When treatment is needed there are several options, although it's not yet clear which might be best. Most doctors use fludarabine as the first treatment, particularly in younger people. It may be given along with an alkylating agent (cyclophosphamide or chlorambucil), with the monoclonal antibody rituximab (Rituxan), or as a combination of all 3 drugs.

While fludarabine is very active against CLL, it can have side effects such as increasing the risk of infections. For people who may have trouble with side effects, such as older people or those with other health problems, an alkylating agent (chlorambucil or cyclophosphamide) may be used instead, either alone or with a steroid drug (such as prednisone).

Doctors are now studying the use of the monoclonal antibodies rituximab or alemtuzumab (Campath) as part of first-line therapy. It's not yet clear how effective they might be on their own, but they are often used along with other drugs.

Other combinations of drugs may also be also used. Some doctors combine cyclophosphamide with other drugs such as vincristine and prednisone. This combination is known as the CVP regimen. If doxorubicin is also included, it is known as the CHOP regimen.

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.

If very high numbers of leukemia cells are causing 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. In this procedure, 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.

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, while older people may 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 wasn't long-lasting, using the same treatment again may not 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.

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 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 other blood 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 CLL alters a patient's immune system in a way that causes it to attack his or her own red blood cells (*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 the American Cancer Society document, *Non-Hodgkin Lymphoma* for more information), but these cases are often hard to treat.

Less often, CLL may transform to *prolymphocytic leukemia* (PLL). 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 the American Cancer Society document, *Leukemia -- Acute Lymphocytic*).

Acute myeloid leukemia (AML) is another rare complication in patients who have been treated for CLL. Drugs such as chlorambucil 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 the American Cancer Society 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 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. One of the purine analog drugs -- cladribine (2-CdA) or pentostatin -- is most often used to treat HCL. 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 difference in the long term.

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).

The American Cancer Society collaborates with the NCCN to produce a version of some of these treatment guidelines, written specifically for patients and their families. These less-technical versions are available on both the NCCN Web site (www.nccn.org) and the ACS Web site (www.cancer.org). A print version can also be requested from the ACS at 1-800-ACS-2345. Treatment guidelines for chronic lymphocytic leukemia (CLL) are included in the "Non-Hodgkin's Lymphoma" 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?
- Should I be treated at this time? Why or why not?
- What treatment choices do I have?
- Which treatment do you recommend, and why?
- What are the risks and side effects with the treatments that you recommend?
- What can I do to help reduce the side effects I may have from the chemotherapy?
- What are the chances that my leukemia will come back after treatment?
- What is the outlook for my survival?

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 second opinions or 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 generally not thought to be curable, although most patients live for many years with the disease, and treatment can extend this even further.

Follow-up Care

You will likely need frequent follow-up exams for many years after treatment, even if there are no signs of the disease. These follow-up visits are very important. Your doctors will continue to watch for signs of recurrent disease, as well as for short-term and long-term side effects of treatment. It is important that you report any new symptoms to the doctor right away so that relapse or side effects can be treated.

Checkups 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 during and after your recovery.

People with CLL are 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 in the office of a new doctor. Your original doctor may have moved or retired, or you may have moved or changed doctors for some reason. It is important that you be able to give your new doctor the exact details of your diagnosis and treatment. Make sure you have the following information handy:

- a copy of your pathology report from any biopsy or surgery
- if you had surgery, a copy of your operative report
- if you were hospitalized, a copy of the discharge summary that every doctor must prepare when patients are sent home from the hospital
- finally, since some drugs can have long-term side effects, a list of your drugs, drug doses, and when you took them

Lifestyle Changes to Consider During and After Treatment

Having cancer and dealing with treatment can be time-consuming and emotionally draining, but it can also 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 begin this process during cancer treatment.

Make Healthier Choices

Think about your life before you learned you had cancer. Were there things you did that might have made you less healthy? Maybe you drank too much alcohol, or ate more than you needed, or smoked, or didn’t exercise very often. Emotionally, maybe you kept your feelings bottled up, or maybe you let stressful situations go on too long.

Now is not the time to feel guilty or to blame yourself. However, you can start making changes today that can have positive effects for the rest of your life. Not only will you feel better but you will also be healthier. What better time than now to take advantage of the motivation you have as a result of going through a life-changing experience like having cancer?

You can start by working on those things that you feel most concerned about. 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's Quitline® tobacco cessation program at 1-800-ACS-2345.

Diet and Nutrition

Eating right can be a challenge for anyone, but it can get even tougher during and after cancer treatment. For instance, treatment often may change your sense of taste. Nausea can be a problem. You may lose your appetite for a while and lose weight when you don't want to. On the other hand, some people gain weight even without eating more. This can be frustrating, too.

If you are losing weight or have taste problems during treatment, do the best you can with eating and remember that these problems usually improve over time. You may want to ask your cancer team for a referral to a dietitian, an expert in nutrition who can give you ideas on how to fight some of the side effects of your treatment. You may also find it helps to eat small portions every 2 to 3 hours until you feel better and can go back to a more normal schedule.

One of the best things you can do after treatment is to put healthy eating habits into place. You will 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 white flour and sugars. Try to limit meats that are high in fat. Cut back on processed meats like hot dogs, bologna, and bacon. Get rid of them altogether if you can. If you drink alcohol, limit yourself to 1 or 2 drinks a day at the most. And don't forget to get some type of regular exercise. The combination of a good diet and regular exercise will help you maintain a healthy weight and keep you feeling more energetic.

Rest, Fatigue, Work, and Exercise

Fatigue is a very common symptom in people being treated for cancer. This is often not an ordinary type of tiredness but a "bone-weary" exhaustion that doesn't get better with rest. For some, this fatigue lasts a long time after treatment, and can discourage them from physical activity.

However, exercise can actually help you reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel physically and emotionally improved and can cope better.

If you are ill and need to be on bed rest during treatment, it is normal to expect your fitness, endurance, and muscle strength to decline some. Physical therapy can help you maintain strength and range of motion in your muscles, which can help fight fatigue and the sense of depression that sometimes comes with feeling so tired.

Any program of 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 3 times a week. If you haven't exercised in a few years but can still get around, you may want to think about taking short walks.

Talk with your health care team before starting, and get their opinion about your exercise plans. Then, try to get an exercise buddy so that 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, though, you will need to balance activity with rest. It is okay to rest when you need to. It is really hard for some people to allow themselves to do that when they are used to working all day or taking care of a household. (For more information about fatigue, please see the publication, *Cancer-Related Fatigue and Anemia Treatment Guidelines for Patients.*)

Exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- It strengthens your muscles.
- It reduces fatigue.
- It lowers anxiety and depression.
- It makes you feel generally happier.
- It helps you feel better about yourself.

And long term, we know that exercise plays a role in preventing some cancers. The American Cancer Society, in its guidelines on physical activity for cancer prevention, recommends that adults take part in at least 1 physical activity for 30 minutes or more on 5 days or more of the week. Children and teens are encouraged to try for at least 60 minutes a day of energetic physical activity on at least 5 days a week.

How About Your Emotional Health?

Once your treatment ends, you may find yourself overwhelmed by 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 your treatment.

Now you may find that you think about the potential of your own death, or the effect of your cancer on your family, friends, and career. You may also begin to re-evaluate your relationship with your spouse or partner. Unexpected issues may also cause concern -- for instance, as you become healthier and have fewer doctor visits, you will see your health care team less often. That can be a source of anxiety for some.

This is an ideal time to seek out emotional and social 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 individual counselors.

Almost everyone who has been through cancer can benefit from getting some type of support. 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 realistic to go it all by yourself. And your friends and family may feel shut out if you decide 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-ACS-2345 and we can put you in touch with an appropriate group or resource.

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 healthy choices and feeling as well as possible, physically and emotionally.

What Happens if Treatment Is No Longer Working?

If cancer continues to grow after one kind of treatment, or if it returns, it is often possible to try another treatment plan that might still cure the cancer, or at least control it enough to help you live longer and feel better. On the other hand, when a person has received several different medical treatments and the cancer has not been cured, over time the cancer tends to become resistant to all treatment. At this time it's important to weigh the possible limited benefit of a new treatment against the possible downsides, including continued doctor visits and treatment side effects.

Everyone has his or her own way of looking at this. Some people may want to try anything possible, while others focus on remaining comfortable during their limited time left.

This is likely to be the most difficult time in your battle with cancer -- when you have tried everything medically within reason and it's just not working anymore. Although your doctor may offer you new treatment, you need to consider that at some point, continuing treatment is not likely to improve your health or change your prognosis or survival.

If you want to continue treatment to fight your cancer as long as you can, you still need to consider the odds of more treatment having any benefit. In many cases, your doctor can estimate the response rate for the treatment you are considering. Some people are tempted to try more chemotherapy or radiation, for example, even when their doctors say that the odds of benefit are less than 1%. In this situation, you need to think about and understand your reasons for choosing this plan.

No matter what you decide to do, it is important that you be as comfortable as possible. Make sure you are asking for and getting treatment for any symptoms you might have, such as pain. This type of treatment is called "palliative" treatment.

Palliative treatment helps relieve these symptoms, but is not expected to cure the disease; its main purpose is to improve your quality of life. Sometimes, the treatments you get to control your symptoms are similar to the treatments used to treat cancer. For example, radiation therapy might be given to help relieve bone pain from bone metastasis. Or chemotherapy might be given to help shrink a tumor and keep it from causing a bowel obstruction. But this is not the same as receiving treatment to try to cure the cancer.

At some point, you may benefit from hospice care. Most of the time, this can be given at home. Your cancer may be causing symptoms or problems that need attention, and hospice focuses on your comfort. You should know that receiving hospice care doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. It just means that the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult stage of your cancer.

Remember also that maintaining hope is important. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that can bring happiness and meaning. In a way, pausing at this time in your cancer treatment is an opportunity to refocus on the most important things in your life. This 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.

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 chronic lymphocytic leukemia (CLL) is providing insight into why these cells grow too quickly, live too long, and fail to develop into normal blood cells. They also help doctors 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 whether or not 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

There are many different drugs now used to treat CLL. Doctors are trying to determine which combinations of these drugs are most effective and offer the best chance for long-term survival.

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 in progress to try to answer these questions.

New Drugs for Chronic Lymphocytic Leukemia

There are dozens of new drugs 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.

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 are used alone to try to prompt the immune system to attack leukemia cells. 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), and is now being studied against both HCL and CLL in clinical trials.

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-ACS-2345.

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

Bone Marrow and Peripheral Blood Stem Cell Transplants

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

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

The following books are available from the American Cancer Society. Call us at 1-800-ACS-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:

Caitlin Raymond International Registry (for unrelated bone marrow transplants)
Telephone: 1-800-726-2824
Internet Address: www.crir.org

Leukemia & Lymphoma Society
Telephone: 1-800-955-4572
Internet Address: www.lls.org

Leukemia Links
Internet Address: www.acor.org/leukemia

National Bone Marrow Transplant Link (nbmtLINK)
Telephone: 1-800-LINK-BMT (1-800-546-5268)
Internet Address: www.nbmtlink.org

National Cancer Institute
Telephone 1-800-4-CANCER (1-800-422-6237)
Internet Address: www.cancer.gov

National Marrow Donor Program
Telephone: 1-800-MARROW-2 (1-800-627-7692)
Internet Address: www.marrow.org

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

The American Cancer Society is happy to address almost any cancer-related topic. If you have any more questions, please call us at 1-800 ACS 2345 at any time, 24 hours a day.

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Last Medical Review: 7/31/2007

Last Revised: 3/22/2008