MAYO CLINIC LABORATORIES

PATIENT EDUCATION

Chronic Lymphocytic Leukemia (CLL)

Introduction

Chronic lymphocytic leukemia (CLL) is a type of cancer of the **lymphocytes** (a kind of white blood cell). It is also referred to as small lymphocytic lymphoma (SLL). CLL/SLL is one of the most common lymphoid cancers in the United States.

The course of CLL/SLL varies a lot. One-third of people with CLL/SLL never need treatment, one-third don't need treatment for many years, and one-third need treatment immediately.

Although currently there is no cure for CLL/SLL, treatment to control the disease is available. New advances in testing make it easier to diagnose CLL/SLL earlier and to better predict how the disease will progress. However, some testing is still only available on a limited basis. If you have been diagnosed with CLL/SLL, it is best to consult with a **hematologist** who is experienced in diagnosing, counseling and treating the disease.

This resource tells you about the following aspects of CLL/SLL:

- Diagnosis
- Prognosis
- Treatment
- Complications

If you have questions about this information or about your condition, talk with your health care provider.

Words in bold are explained in a word list at the end of this resource.

What is chronic lymphocytic leukemia/small lymphocytic lymphoma?

CLL/SLL is a cancer of the lymphocytes (one kind of white blood cell that impacts your immune system). In order to understand CLL, it may help to learn some general information about your blood and lymphatic system.

Your blood

Normally, your body's **bone marrow** produces stem cells that grow into different types of blood cells (figure 1). Three types of mature blood cells are:

- **Red blood cells** (erythrocytes) that carry oxygen from your lungs to all parts of your body. In order to work well, your body needs a constant supply of oxygenated blood.
- **Platelets** that help your blood clot after a cut or an injury.
- **White blood cells** (leukocytes) that fight infection and disease.

One kind of white blood cell is a lymphocyte. There are three kinds of lymphocytes:

- **B lymphocytes**
- T lymphocytes
- Natural killer cells

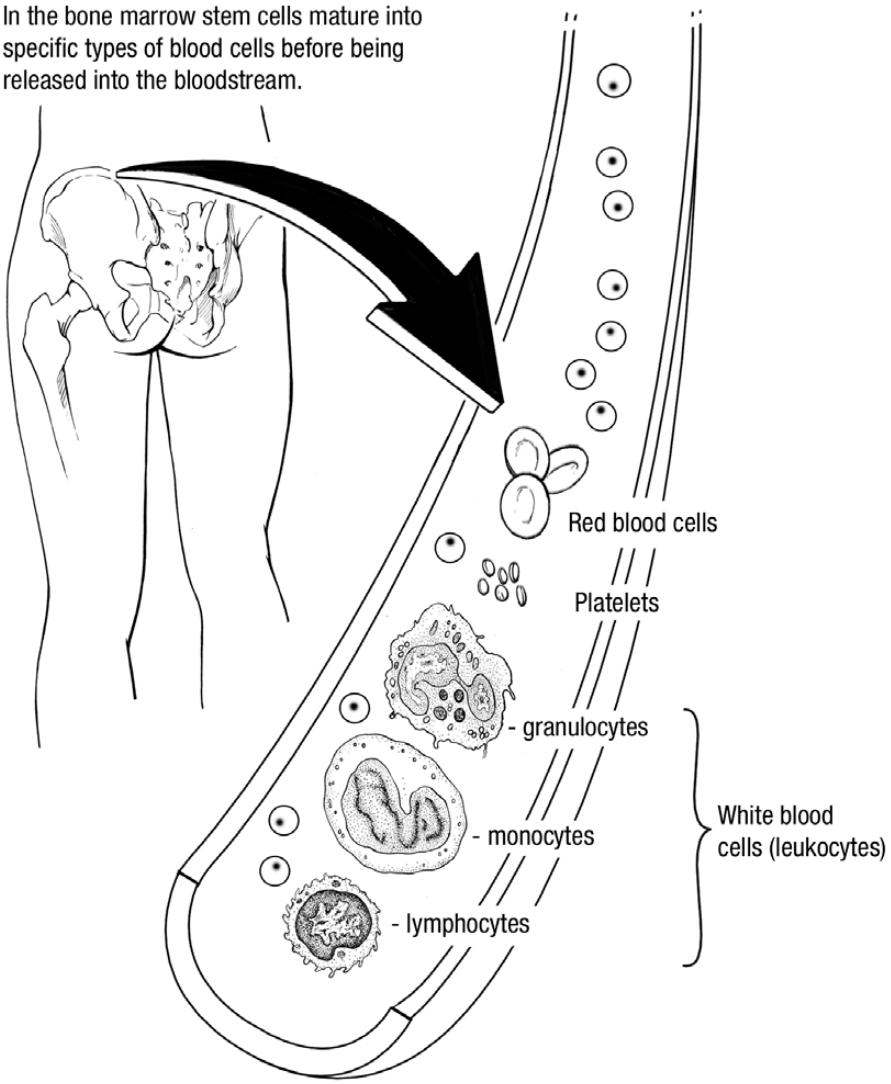

Figure 1. Blood cells

CLL/SLL is caused when the B lymphocytes that come from a single, abnormal cell accumulate. Because of damage to their DNA, the lymphocytes grow in an uncontrolled manner and live longer than normal. This results in a higher than normal concentration of lymphocytes in the blood, bone marrow, lymph nodes and **spleen** (figures 2a, b). These abnormal B lymphocytes tend to crowd out other healthy blood cells, preventing them from doing their normal jobs, including fighting infections.

Lymphatic system

The lymphatic system is part of your immune system and is made up of branches that go to lymph nodes all over your body. It drains body fluid (lymph) from the tissues into the veins. The lymph ducts drain lymph through the lymph nodes, which filter germs and other foreign substances. Lymphocytes and other immune system cells circulate continuously through the tissues, lymph nodes and the bone marrow. When you have an infection, the lymphocytes in the lymph nodes respond to fight the infection and prevent further spread of disease. When activated, lymph nodes can swell. Increased lymph node size also can be a sign of malignancy.

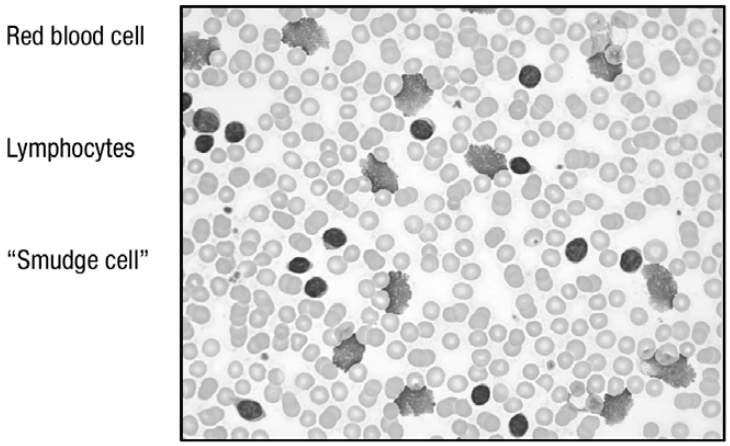

Figure 2a. Magnified view of blood smear from a patient with CLL. Most of the cells are normal red blood cells. In contrast to normal blood, in which the majority of white blood cells are neutrophils, all of these white blood cells are lymphocytes. The smaller white blood cells are intact lymphocytes (CLL cells) and cannot be distinguished from normal lymphocytes. The larger white blood cells are lymphocytes that have been broken by the process of making the blood smear. The "smudge cells" are characteristic of CLL.

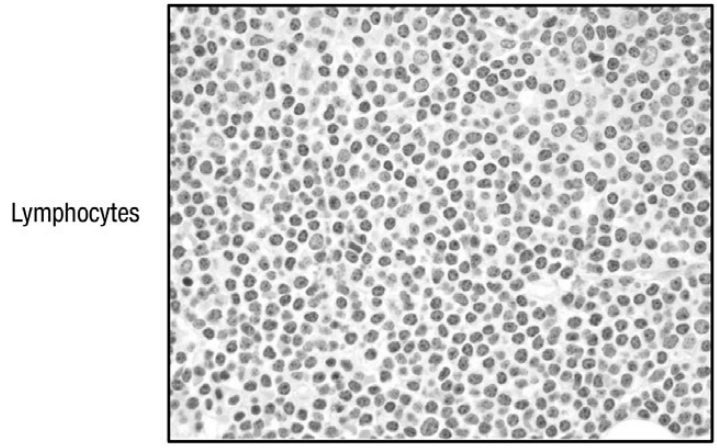

Figure 2b. Magnified view of a section of a bone marrow biopsy. The normal bone marrow cells and fat spaces have been replaced by a monotonous infiltrate of small lymphocytes (CLL cells).

Cause/Risk Factors

The cause for CLL/SLL is not known. Although environmental factors have been suspected, there is no scientific proof that the disease is caused by exposure to toxins.

Risk for CLL/SLL can be inherited although most people with CLL do not have a clear family history of leukemia or lymphoma. If you have a family member with CLL/SLL or another kind of lymphocytic malignancy, you may be more likely to get CLL/SLL. Also, people of European descent are more likely to get the disease.

Your risk increases with age. CLL/SLL is never found in children and rarely found in anyone under 40. The average age of diagnosis is 64. Slightly more men than women get the disease.

Diagnosis and Prognosis

CLL/SLL can be hard to diagnose. Most often, people have no symptoms at first, and the disease is found during routine blood tests that show a high lymphocyte count (ALC or absolute lymphocyte count). Today, the diagnosis can be made earlier than in the past because of improved methods to detect the CLL B cells.

If you have a high white blood cell count, further tests need to be done to diagnose CLL/SLL and exclude other forms of chronic leukemia.

If you have symptoms, they may include:

- Fever
- Drenching night sweats
- Unintended weight loss
- Fatigue
- Frequent infections
- Enlarged spleen or liver
- Enlarged lymph nodes
- **Autoimmune** complications

It is very important to diagnose CLL/SLL accurately. An accurate diagnosis is needed in order to have an idea about the progression of the disease (the prognosis) and the best treatment options.

A complete physical examination with a medical history is done. Blood tests can help to confirm the diagnosis and to provide information about the possible progression of the disease. Blood tests that may be done include:

- **CBC (complete blood count).** This is needed to measure the effect of the disease on normal blood cell production. By doing a CBC every three to six months, it may be possible to calculate the lymphocyte doubling time (LDT), which measures how long it takes the absolute lymphocyte count (ALC) to double. A shorter LDT (less than one year) seems to be related to a more aggressive disease.
- F**low cytometry examination of blood cells.** Usually, this is the standard way to diagnose CLL/SLL. Cells are examined with antibodies, which show if they are malignant and if they have characteristics of CLL/SLL. Levels of cellular proteins, ZAP-70 and CD38, are also examined. High levels of either of these proteins may predict a poorer prognosis. Flow cytometry is available from Mayo Clinic Laboratories as Mayo ID: LCMS / Leukemia/Lymphoma Immunophenotyping by Flow Cytometry. This limited panel, together with the patient history is used to determine what, if any, further testing is needed for disease diagnosis or classification.

- **FISH (fluorescence in situ hybridization) panel.** This is a way of looking at **chromosomal** abnormalities (figure 3) that may occur more often in people with CLL/SLL. Some types of abnormalities seem to predict a more aggressive disease course.

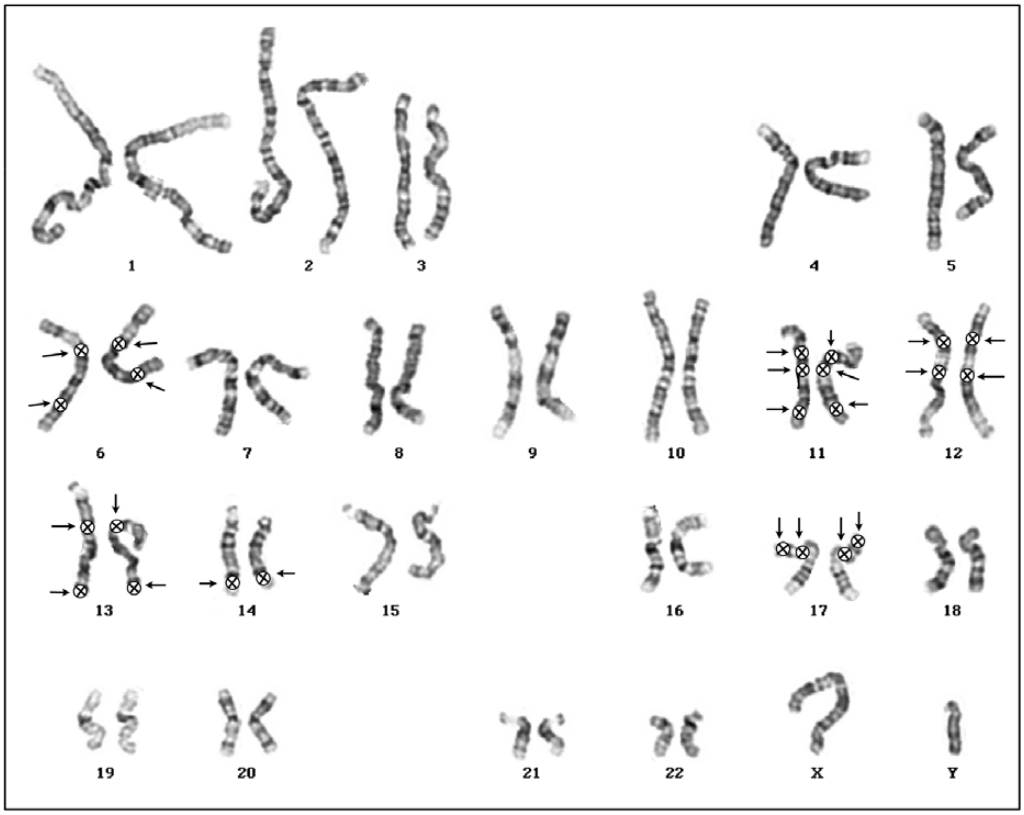

Figure 3. Chromosome defects in CLL most often affect chromosomes 6, 11, 12, 13, and 17. This photograph shows the binding sites for the FISH probes used to study these chromosomes. The chromosome 14 probe is used to ensure that patients do not have mantle cell lymphoma.

- **IgV_H (immunoglobulin variable region of the heavy chain) mutation status.** Normal B lymphocytes undergo additional mutations (changes) in the **gene** for their **antibody** as part of the normal immune response to infection. These mutations increase the effectiveness of the antibodies produced by the body. In people with CLL/SLL, the abnormal B lymphocytes can be tested for additional mutations. More mutations of the antibody gene over a certain percent may be associated with a better prognosis.

A bone marrow biopsy is not required to diagnose CLL/SLL, but it can provide valuable information about the possible course of CLL in some cases. Bone marrow examination may be done before starting treatment for CLL/SLL.

Some of the tests mentioned here are not widely available. If you have been diagnosed with possible CLL/SLL, you may wish to consult with a hematologist who has experience in the diagnosis and treatment of this disease. Tests done depend on your individual situation. If you have questions about tests, talk with your health care provider.

Staging

After the diagnosis of CLL/SLL is confirmed, staging may be done. Staging is done to help predict how the disease will progress. Two common staging systems are the Rai and Binet systems. The Rai staging is now divided into three stages: low risk, intermediate risk, or high risk.

Staging looks at:

- Number and location of affected lymph nodes
- **Hemoglobin** level
- Platelet counts
- Spleen and liver size

Other factors, including age and overall state of health also influence the prognosis of CLL/SLL. It is important to tell your health care provider about any diseases (diabetes, high blood pressure, lung disease) you have because they may impact treatment decisions.

Living with CLL/SLL

Being diagnosed with CLL/SLL can be stressful because of the potential seriousness of the disease and the uncertainty about the outcome. Talk to your health care provider about support groups and other resources available to help you and your family cope with a diagnosis of CLL/SLL.

Summary

Although staging is still used to help determine the prognosis of people with CLL/SLL, some of the newer tests discussed above seem to be more useful in predicting the risk of progression in people with early stage disease.

However, some of these tests are not widely available. Look for a medical center with hematologists experienced in the diagnosis and treatment of CLL/SLL.

Treatment

There is currently no cure for CLL/SLL; the goal of treatment is to manage the disease—to ease symptoms and to prolong life. Treatment options depend on the results of the blood tests, the staging of the disease, the symptoms and the overall health of the patient.

Treatment options are changing rapidly.
Possible treatments include:

- **Observation.** If you have no symptoms and tests show that you are at low risk for the disease to progress, you may not need any treatment—at least at first. However, even if you don't need treatment when you are first diagnosed, it is important that you follow the recommendations of your health care provider regarding follow-up. You may need only observation for years if no symptoms develop. Your health care provider also may recommend changes in your lifestyle to promote good health.
- **Chemotherapy.** Chemotherapy may be one drug or a combination of drugs. Chemotherapy affects the whole body, so a patient can have significant side effects.
- **Biological therapy** (this includes, but is not restricted to, monoclonal antibody therapy). This is targeted therapy; for example, antibodies target lymphocytes, so treatment may be less toxic and there are fewer side effects than with chemotherapy. Monoclonal antibodies may be combined with chemotherapy. Some recent combinations have shown a better response than the use of chemotherapy alone.
- **Hematopoietic stem cell transplant (bone marrow transplant)** is an emerging therapy that may be considered for high-risk patients. It uses chemotherapy and/or radiation therapy along with the infusion of non-embryonic stem cells from a tissue-matched donor. This may act on the leukemia through both the effect of the chemotherapy and/or the radiation therapy and through the effects of the donor cells.

Note on complementary therapy. People often turn to complementary therapies for CLL/SLL. Most of these therapies have not been formally tested, and their effectiveness is unknown. Some complementary therapies can interfere with other medications. To avoid possible toxic reactions, tell your health care provider if you are using any complementary therapy—especially if your CLL is being treated with conventional therapies.

Treatment for CLL/SLL is changing quickly. Effective, innovative treatment depends on an accurate diagnosis of the disease. Clinical trials are constantly going on. If you have questions about treatment or clinical trials, talk with your health care provider.

Healthy Lifestyle

To maximize your quality of life if you have CLL/SLL, your health care provider may recommend certain guidelines for daily living. Healthy approaches to diet, exercise and personal habits may improve long-term survival. If you have questions about activities of daily living, talk with a member of your health care team.

Smoking

Not using tobacco or deciding to stop using it is one of the most important health decisions you can make. Using any type of tobacco—cigarettes, snuff, pipe tobacco or cigars—greatly increases your chance of getting cancer. If you use tobacco, your heart, lungs and blood vessels don't work as well.

Nutrition

Follow a "heart-healthy" diet that includes low to moderate use of fat, sugar and salt and maintain a healthy weight. Maintaining a healthy weight is a lifelong commitment, requiring healthy food choices and exercise. Healthy food choices include the following:

- At least five fruit and vegetable servings each day
- Adequate fiber (whole-grain and enriched cereals, breads and other foods made from whole grain)
- Low-fat or skim milk and low-fat dairy products
- Lean meats, fish and poultry

Alcohol use

Follow the recommendations of your health care team regarding use of alcohol.

Activity

Physical activity may help to keep your body fit. Talk to your health care provider about guidelines for an exercise program.

Hand washing

Hand washing is the most effective way to prevent the spread of infection. Always wash your hands after using the bathroom, before eating and when you handle food. Wash your hands more often if you are sick or if you are around a sick person.

Screening

If you have CLL/SLL, you have an increased risk for other cancers. Follow these guidelines for cancer prevention and screening:

Skin

- Use sunscreen (30 SPF or higher).
- Avoid prolonged sun exposure.
- See a dermatologist about new or changing skin lesions, or as recommended by your health care provider.

Breast

- Do a monthly self-exam.
- Have an annual breast exam by a health care provider.
- Have regular mammograms (either annually after age 40 or as indicated by family history).

Cervical

- Have a Pap smear annually.

Prostate

- Have a digital rectal exam annually.
- Get a PSA (prostate-specific antigen) blood test annually over age 50 unless your health care provider tells you otherwise.

Colon

- Starting at age 50, get a colonoscopy as recommended by your health care provider.

Immunizations

Discuss immunizations with a member of your health care team. Some immunizations are specifically recommended for people who are more susceptible to infections.

Complications

If you have CLL/SLL, you may also have some of the following complications:

- Recurrent infections
- **Autoimmune diseases** [examples include autoimmune hemolytic anemia and immune thrombocytopenic purpura (ITP)]
- Increased risk of second cancers, including more aggressive lymphoma, aggressive skin cancer or solid tumors

Possible complications resulting from CLL/SLL or treatment for the disease are difficult to predict. If you have questions about complications of CLL/SLL, talk with your health care provider.

Research

Many clinical research studies currently are being done on CLL/SLL. You may be asked to participate in a clinical research study. Researchers design studies to better understand the causes and progression of CLL/SLL and to test the safety and effectiveness of different treatments. Some studies test treatments that have been proven, comparing them to other forms of therapy to see which ones are better.

However, the decision whether or not to take part in a study is entirely up to you. If you are asked to participate in a study, be sure you understand the study's purpose and risks, how long it will last and your responsibilities. Know that you can stop at any time and that your decision—either to participate or not or to stop—in no way affects your medical care.

If you have questions about a study, speak with your health care provider.

Word List

Antibody—Substance that the body makes to help protect itself from foreign cells.

Autoimmune disease—Disease that occurs when antibodies that are formed to fight infection react against the body's own normal tissue. (Examples include rheumatoid arthritis, autoimmune hemolytic anemia, immune thrombocytopenic purpura).

B lymphocyte—(also called B-cell). Cell made in the bone marrow that works as part of the immune system. B lymphocytes make antibodies to fight infection.

Bone marrow—Soft tissue located in the center of the bones where blood is made.

Chemotherapy—Use of drugs to kill malignant cells.

Chromosome—Structure in the center of a cell that is made up of DNA and protein and contains genes.

Gene—Structure within a chromosome that is responsible for the inheritance of a particular characteristic.

Hematologist—Specialist in the science that deals with blood and tissues that make blood.

Hemoglobin—Iron-containing pigment of the red blood cell that carries oxygen to the tissues.

Lymph nodes—Widely distributed throughout your body, these make up a significant part of your immune system.

Lymphocytes—An important part of the immune system, a type of white blood cell that fights infection.

Mutation—Change in a gene that results from a change to the DNA coding sequences in a cell.

Platelets—Type of blood cell that contributes to clotting.

Red blood cells (erythrocytes)—Contain hemoglobin, which carries oxygen to the body.

Spleen—Organ in your abdomen that is part of the lymphoid system that contains lymphocytes and plasma cells.

White blood cells (leukocytes)—Part of the blood that fights infection.

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