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Chronic Lymphocytic Leukemia Early Detection, Diagnosis, and Staging

Know the signs and symptoms of chronic lymphocytic leukemia. Find out how CLL is tested for, diagnosed, and staged.

Detection and Diagnosis

Finding cancer early often allows for more treatment options. Some early cancers may have signs and symptoms that can be noticed, but that's not always the case.

- [Can Chronic Lymphocytic Leukemia Be Found Early?](#)
- [Signs and Symptoms of Chronic Lymphocytic Leukemia](#)
- [Tests for Chronic Lymphocytic Leukemia \(CLL\)](#)

Stages and Outlook (Prognosis)

After a cancer diagnosis, staging provides important information about the extent of cancer in the body and anticipated response to treatment.

- [How Is Chronic Lymphocytic Leukemia Staged?](#)

Questions to Ask About CLL

Here are some questions you can ask your cancer care team to help you better understand your CLL diagnosis and treatment options.

- [Questions to Ask About Chronic Lymphocytic Leukemia](#)

Can Chronic Lymphocytic Leukemia Be Found Early?

For certain cancers, the [American Cancer Society recommends screening tests](#)¹ in people without any symptoms, because they are easier to treat if found early. But for chronic lymphocytic leukemia (CLL), no screening tests are routinely recommended at this time.

Many times, CLL is found when routine blood tests are done for other reasons. For instance, a person's white blood cell count may be very high, even though they don't have any symptoms.

If you notice any [symptoms that could be caused by CLL](#), report them to your doctor right away so the cause can be found and treated, if needed.

Hyperlinks

1. www.cancer.org/cancer/screening/american-cancer-society-guidelines-for-the-early-detection-of-cancer.html

Last Revised: May 10, 2018

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](#)¹ for

some unrelated health problem or during a routine check-up and they are found to have a high number of lymphocytes.

Even when people with CLL have symptoms, they're often vague and can be symptoms of other things. Overall, the signs and symptoms of leukemia can affect men or women and do not differ by sex or gender. Symptoms can include the following:

- Weakness
- [Feeling tired](#)²
- Weight loss
- Chills
- Fever
- Night sweats
- Swollen lymph nodes (often felt as lumps under the skin)
- Pain or a sense of "fullness" in the belly (this can make someone feel full after only a small meal), which is caused by an enlarged spleen and/or liver

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 don't have 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](#)³. You might hear the term **neutropenia**, which refers to low levels of neutrophils (a type of granulocyte needed to fight bacterial infections). People with CLL may have very high white blood cell counts because of excess numbers of lymphocytes (**lymphocytosis**), but the leukemia cells don't fight infection the way normal white blood cells do.
- A shortage of blood platelets (**thrombocytopenia**) can lead to excess bruising, bleeding, frequent or severe nosebleeds, and bleeding gums.

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

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

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

Hyperlinks

1. www.cancer.org/cancer/diagnosis-staging/tests/understanding-your-lab-test-results.html
2. www.cancer.org/cancer/managing-cancer/side-effects/fatigue.html
3. www.cancer.org/cancer/managing-cancer/side-effects/infections.html

References

American Society of Clinical Oncology. Leukemia - Chronic Lymphocytic - CLL: Symptoms and Signs (06/2016). Accessed at www.cancer.net/cancer-types/leukemia-chronic-lymphocytic-cll/symptoms-and-signs on April 12, 2018.

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Last Revised: February 27, 2024

Tests for Chronic Lymphocytic Leukemia (CLL)

Certain [signs and symptoms](#) or the results of blood tests (see below) might suggest that a person has chronic lymphocytic leukemia (CLL), but further tests are needed to be sure. If CLL is found, other tests will also be done to learn more about it.

- [Medical history and physical exam](#)
- [Blood tests](#)
- [Lymph node biopsy](#)
- [Bone marrow aspiration and biopsy](#)
- [Lab tests of blood and biopsy samples](#)
- [Imaging tests](#)

Medical history and physical exam

If you might have CLL (or some other type of leukemia), your doctor will want to take a complete **medical history**, focusing on any symptoms you've had and how long you've had them. They might also ask about other health problems, as well as about possible [risk factors for CLL](#)¹.

During the **physical exam**, your doctor will pay close attention to your lymph nodes, abdomen (belly), and other areas that might be affected.

If there is reason to think you might have problems caused by low levels of blood cells (anemia, infections, bleeding or bruising, etc.), the doctor will most likely order tests to check your blood cell counts. If the results suggest leukemia, you may be referred to a **hematologist**, a doctor who specializes in treating blood disorders (including blood cancers like leukemia).

Blood tests

Most often, CLL can be diagnosed based on the results of blood tests (taken from a vein in the arm). Other blood tests might also be done to learn more about the leukemia and about a person's overall health.

Complete blood count and peripheral blood smear

The [complete blood count \(CBC\)](#)² measures the amounts of red and white cells and platelets in your blood. This test is often done along with one that looks at the numbers of the different types of white blood cells (called a **differential** or **diff**). These tests are often the first ones done when a blood problem is suspected.

People with CLL have too many lymphocytes in their blood. (This is called **lymphocytosis**.) Having more than 5,000 lymphocytes/mm³ (per cubic millimeter) of blood strongly suggests CLL, but other tests are needed to know for sure. People with CLL might also have low levels of red blood cells and platelets.

For the **peripheral blood smear**, a sample of blood is looked at with a microscope. If you have CLL, the blood smear could show many abnormal looking lymphocytes called **smudge cells**.

Flow cytometry

This lab test is important in diagnosing CLL. It uses a machine that looks for certain substances (markers) on or in cells that help identify what types of cells they are.

Flow cytometry can be used to see if a sample of blood contains CLL cells. It can also be used to look for CLL cells in bone marrow or other fluids. (See below.) If a person has CLL, the test will show that the leukemia cells are all the same, and that they have certain markers.

Other blood tests

Blood chemistry tests may be done to measure the amount of certain chemicals in your blood, but they're not used to diagnose leukemia. In people already known to have CLL, these tests can help find liver or kidney problems caused by the spread of leukemia cells or certain chemotherapy (chemo) drugs. These tests also can check the levels of certain minerals so any imbalances can be treated.

Your doctor may order blood tests to check for **previous hepatitis virus infections** if you're going to be treated with a drug that might reactivate these infections. (You can find more on this in [Immunotherapy for Chronic Lymphocytic Leukemia³](#).)

Your blood **immunoglobulin (antibody) levels** may be tested to check if you have enough antibodies to fight infections, especially if you've recently had a lot of infections.

A blood protein called **beta-2-microglobulin** may be measured. High levels of this protein generally mean a more advanced CLL.

Lymph node biopsy

In a lymph node biopsy, all or part of a lymph node is removed so it can be looked at under a microscope and tested to see if it contains leukemia cells.

This test isn't always needed to diagnose CLL, but it might be done if the results of blood tests aren't enough to make the diagnosis. A lymph node biopsy may also be done if a lymph node has grown very large and the doctor wants to know if the leukemia has changed (transformed) into a more aggressive type of cancer.

Lymph node biopsies can be done in different ways.

In an **excisional lymph node biopsy**, an entire lymph node is removed through a cut in the skin. If the lymph node is very large, only part of it may be removed using an **incisional biopsy**. If the node is near the skin surface, this is a simple operation that can be done by first numbing the skin, but if the node is inside the chest or abdomen (belly), general anesthesia (where the patient is in a deep sleep) is used.

Less often, a needle biopsy may be done, either using a very thin, hollow needle (**a fine needle aspiration**, or **FNA**) or a slightly larger hollow needle (**a core needle biopsy**, or **CNB**). But it can be harder to diagnose CLL from a needle biopsy.

Bone marrow aspiration and biopsy

Blood tests or a lymph node biopsy are often enough to diagnose CLL, but if not, samples of bone marrow (the inner parts of certain bones, where new blood cells are made) might be tested.

A **bone marrow aspiration and biopsy** are usually done together. The samples of bone marrow are usually taken from the back of the pelvic (hip) bone, but sometimes they may be taken from other bones.

For a **bone marrow aspiration**, you lie on a table (either on your side or on your belly). After cleaning the skin over your hip, the doctor uses a thin needle to put in a drug that numbs the area and the surface of the bone. This may cause brief stinging or burning. A hollow needle is then put into the bone, and a syringe is used to suck out a small amount of liquid bone marrow. Even with the numbing medicine, most people still have some brief pain when the marrow is removed.

A **bone marrow biopsy** is usually done just after the aspiration. A small piece (core) of bone and marrow is removed with a larger needle that's pushed down into the bone. Even with the numbing medicine, this can cause a feeling of pressure or tugging, but it usually doesn't hurt. After the biopsy is done, pressure will be put the site to help prevent bleeding.

Lab tests of blood and biopsy samples

Different types of lab tests might be done on blood or biopsy samples.

Routine microscopic exams

Samples from blood or biopsies are looked at under a microscope by a **pathologist** (a doctor specializing in lab tests) and may be reviewed by the patient's **hematologist/oncologist** (a doctor specializing in cancer and blood diseases).

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.

A key factor is if the cells look mature (like normal blood cells that can fight infections). CLL cells tend to look mature, while cells of acute leukemias look immature.

Flow cytometry and immunohistochemistry

For both flow cytometry (as mentioned above) and immunohistochemistry (IHC), samples of cells are treated with antibodies, which are proteins that stick only to certain other proteins on cells. For IHC, the cells are then looked at with a microscope to see if the antibodies stuck to them (meaning they have these proteins), while for flow cytometry a special machine is used.

These tests are used for classifying leukemia cells according to the substances (antigens or markers) on their surfaces (a process called **immunophenotyping**). Leukemia cells can have different markers depending on which type of cells they start in and how mature they are, so this information can be helpful in diagnosing CLL or learning more about it.

Fluorescent in situ hybridization (FISH): This test can be used to look at the cells' chromosomes and DNA without having to grow the cells in the lab. It uses special fluorescent dyes that only attach to specific parts of particular chromosomes. FISH can be used to look for certain genes or chromosome changes (not just any change). Because the cells don't have to grow in the lab first, the results are usually available faster than with cytogenetics, often within a few days.

What these tests look for

In people with CLL, the leukemia cells often have certain chromosome changes. For example, part of a chromosome may be missing. This is called a **deletion**. The most common deletions occur in parts of chromosomes 13, 11, or 17. Other, less common chromosome changes include an extra copy of chromosome 12 (trisomy 12) or a translocation (swapping of DNA) between chromosomes 11 and 14, written as **t(11;14)**.

This type of information may be helpful to determine a person's prognosis (outlook). For example, the deletion of part of chromosome 13, written as **del(13q14)**, is usually linked with a slower-growing disease and a better outlook, while a deletion of part of chromosome 17, written as **del(17p)**, often means the leukemia is less likely to respond to certain kinds of treatment. But this information needs to be looked at along with other factors, such as the [stage of the CLL](#).

Molecular and genetic tests

Other types of lab tests can also be done on the samples to look for specific gene or other changes in the leukemia cells. Some of the changes found on these tests can help doctors learn more about the leukemia, and some can even help tell if certain treatments are likely to be helpful. For example:

- Immunoglobulins, the antibodies that help your body fight infections, are made up of light chains and heavy chains. Whether the gene for the immunoglobulin heavy chain variable region (**IGHV** or **IgV_H**) has changed (mutated) can help your doctor know how aggressive your CLL is.
- **TP53** is a gene that normally helps keep cells from growing out of control. Changes (mutations) in this gene tend to be linked with a poorer outlook, and they can affect which treatments are most likely to be helpful.

To learn more about these lab tests, see [Tests Used on Biopsy and Cytology Samples to Diagnose and Classify Cancer](#)⁴.

Imaging tests

Imaging tests use x-rays, sound waves, or magnetic fields to create pictures of the inside of the body. Imaging tests are not done to diagnose CLL, but they may be done for other reasons, such as to look for the cause of symptoms such as chest pain or trouble breathing.

Computed tomography (CT) scan

A [CT scan](#)⁵ can show if any lymph nodes or organs in your body are enlarged. It may be done if your doctor suspects the leukemia is growing in an organ, like your spleen.

PET/CT scan

Some machines combine a CT scan with a [PET scan](#)⁶ (PET/CT scan). For a PET scan, glucose (a form of sugar) containing a radioactive atom is injected into the blood. Because cancer cells grow rapidly, they absorb large amounts of the radioactive sugar. A special camera can then create a picture of the areas of radioactivity in the body. This test allows the doctor to compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT. This test might be used to guide a biopsy needle into a lymph node to remove a sample for testing.

Ultrasound

[Ultrasound](#)⁷ uses sound waves and their echoes to make pictures of the inside of the body. It can be used to look at lymph nodes near the surface of the body or to look for enlarged organs (like the liver and spleen) inside your abdomen.

Hyperlinks

- [biopsy-and-cytology-samples-for-cancer/special-tests.html](#)
5. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ct-scan-for-cancer.html
 6. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/nuclear-medicine-scans-for-cancer.html
 7. www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/ultrasound-for-cancer.html

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Rai KR, Stilgenbauer S. Staging and prognosis of chronic lymphocytic leukemia. UpToDate. 2024. Accessed at <https://www.uptodate.com/contents/staging-and-prognosis-of-chronic-lymphocytic-leukemia> on June 7, 2024.

Rai KR, Stilgenbauer S, Aster JC. Clinical features and diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma. UpToDate. 2024. Accessed at <https://www.uptodate.com/contents/clinical-features-and-diagnosis-of-chronic-lymphocytic-leukemia-small-lymphocytic-lymphoma> on June 7, 2024.

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How Is Chronic Lymphocytic Leukemia Staged?

- [Staging systems for chronic lymphocytic leukemia](#)
- [Prognostic factors for chronic lymphocytic leukemia](#)
- [Staging for hairy cell leukemia](#)
- [Monoclonal B-lymphocytosis](#)
- [Small lymphocytic lymphoma](#)

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

Chronic lymphocytic leukemia (CLL), on the other hand, does not usually form tumors. It's generally in the bone marrow and blood. And, in many cases, it has spread to other organs such as the spleen, liver, and lymph nodes by the time it's found. The outlook for a person with CLL depends on other information, such as the results of lab test and imaging tests.

Staging systems for chronic lymphocytic leukemia

A staging system is a standard way for the cancer care team to describe cancer. There are 2 different systems for staging CLL:

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

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

Rai staging system

The Rai system is based on lymphocytosis. The patient must have a high number of lymphocytes in their blood and bone marrow that isn't linked to any other cause (like infection).

For a diagnosis of CLL, the overall lymphocyte count does not have to be high, but the patient must have at least 5,000/mm³ monoclonal lymphocytes (sometimes called a

monoclonal lymphocytosis). Monoclonal means that the cancer cells all came from one original cell. This causes them to have the same chemical pattern which can be seen with special testing.

This system divides CLL into 5 stages based on the results of blood tests and a physical exam:

- **Rai stage 0:** Lymphocytosis; no enlargement of the lymph nodes, spleen, or liver; red blood cell and platelet counts are near normal.
- **Rai stage I:** Lymphocytosis; enlarged lymph nodes; spleen and liver are not enlarged; red blood cell and platelet counts are near normal.
- **Rai stage II:** Lymphocytosis; enlarged spleen (and maybe an enlarged liver); lymph nodes may or may not be enlarged; red blood cell and platelet counts are near normal.
- **Rai stage III:** Lymphocytosis; lymph nodes, spleen, or liver may or may not be enlarged; red blood cell counts are low (anemia); platelet counts are near normal.
- **Rai stage IV:** Lymphocytosis; enlarged lymph nodes, spleen, or liver; red blood cell counts may be low or near normal; platelet counts are low (thrombocytopenia).

Doctors separate the Rai stages into low-, intermediate-, and high-risk groups when determining treatment options.

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

These risk groups are used later in [Treatment of Chronic Lymphocytic Leukemia](#).¹

Binet staging system

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

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

- **Binet stage C:** Anemia and/or thrombocytopenia are present. Any number of lymphoid tissue areas may be enlarged.

30%)

- CLL cells with a mutated gene for IGHV

Certain prognostic factors such as the presence or absence of ZAP-70, CD38, and a mutated gene for IGHV help divide cases of CLL into 2 groups, slow growing and fast growing. People with the slower growing kind of CLL tend to live longer and may be able to delay treatment longer as well.

Staging for hairy cell leukemia

There is no standard staging system for hairy cell leukemia.

Monoclonal B-lymphocytosis

Some people have monoclonal lymphocytes in their blood, but not enough to make the diagnosis of CLL. If someone has less than 5,000 monoclonal lymphocytes (per mm³), normal counts of red blood cells and platelets, and no enlarged lymph nodes (or enlarged spleen), they have a condition called monoclonal B-lymphocytosis (MBL). MBL doesn't need to be treated, but about one patient of every 100 with this condition will go on to need treatment for CLL.

Small lymphocytic lymphoma

The cancer cells of small lymphocytic lymphoma (SLL) and CLL look the same under the microscope and have the same marker proteins on the surface of the cells. Whether someone is diagnosed with SLL or CLL depends largely on the number of lymphocytes in the blood. To be diagnosed with CLL, there must be at least 5,000 monoclonal lymphocytes (per mm³) in the blood. For it to be called SLL, the patient must have enlarged lymph nodes or an enlarged spleen with fewer than 5,000 lymphocytes (per mm³) in the blood. Still, since SLL and CLL can be treated the same, the difference between them isn't really important.

Hyperlinks

1. www.cancer.org/cancer/types/chronic-lymphocytic-leukemia/treating.html

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Questions to Ask About Chronic

Lymphocytic Leukemia

- [When you're told you have chronic lymphocytic leukemia](#)
- [When deciding on a treatment plan](#)
- [During treatment](#)
- [After treatment](#)

As you cope with chronic lymphocytic leukemia (CLL) and treatment, you need to have honest, open discussions with your doctor. You should feel comfortable asking about anything, 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 give you answers.

When you're told you have chronic lymphocytic leukemia

- What is the [stage](#) (risk group) of the CLL, and what does that mean for me?
- Will I need to have other [tests](#) before we can decide on treatment?
- How much experience do you have treating this type of cancer?
- Should I get a second opinion ?

When deciding on a treatment plan

- Should I start treatment now? Why or why not?
- What are my [treatment choices](#)¹?
- What do you recommend, and why?
- What are the risks and side effects with the treatments that you recommend?
- How often will you test my blood or bone marrow to see how treatment is working?
- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- How will treatment affect my daily activities?
- What is the outlook for my survival?

During treatment

Once treatment begins, you'll need to know what to expect and what to look for. Not all

of these questions may apply to you, but getting answers to the ones that do may be helpful.

- How will we know if the treatment is working?
- Is there anything I can do to help manage side effects?
- What symptoms or side effects should I tell you about right away?
- How can I reach your office on nights, holidays, or weekends?
- Are there any limits on what I can do?
- Can you suggest a mental health professional I can see if I start to feel overwhelmed, depressed, or distressed?

After treatment

- What symptoms should I watch for?
- What will we do if the treatment doesn't work or if the leukemia comes back?
- What will my options be if the leukemia comes back?
- What type of [follow-up](#)² will I need after treatment?
- When can I return to work?

Be sure to write down any questions you have that are not on this list. For instance, you might want information about how you'll feel so that you can plan your work schedule. Or you may want to ask about qualifying for [clinical trials](#)³.

Taking another person with you and/or recording your talks with your doctor can be helpful. Collecting copies of your medical records, pathology reports, and radiology reports is a good idea too.

Hyperlinks

1. www.cancer.org/cancer/types/chronic-lymphocytic-leukemia/treating.html
2. www.cancer.org/cancer/types/chronic-lymphocytic-leukemia/after-treatment/follow-up.html
3. www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html

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