



# Acute Lymphocytic Leukemia Early Detection, Diagnosis, and Types

## Detection and Diagnosis

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

- [Can Acute Lymphocytic Leukemia Be Found Early?](#)
- [Signs and Symptoms of Acute Lymphocytic Leukemia](#)
- [How Is Acute Lymphocytic Leukemia Diagnosed?](#)

## Types of ALL

Learn how ALL is classified and how this may affect your treatment options.

- [How Is Acute Lymphocytic Leukemia Classified?](#)

## Questions to Ask About ALL

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

- [What Should You Ask Your Doctor About Acute Lymphocytic Leukemia?](#)

# Can Acute Lymphocytic Leukemia Be Found Early?

For many types of cancers, diagnosis at the earliest possible stage makes treatment much more effective. The American Cancer Society recommends [screening tests for](#)

[early detection of certain cancers](#) in people without any symptoms.

But at this time there are no special tests recommended to detect acute lymphocytic leukemia (ALL) early. The best way to find leukemia early is to report any possible signs or symptoms of leukemia (see [Signs and symptoms of acute lymphoblastic leukemia](#)) to the doctor right away.

Some people are known to have [a higher risk](#) of ALL (or other leukemias) because of an inherited disorder such as Down syndrome. Most doctors recommend that these people have careful, regular medical checkups. The risk of leukemia, although greater than in the general population, is still very low for most of these syndromes.

- [References](#)

[See all references for Acute Lymphocytic Leukemia](#)

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## Signs and Symptoms of Acute Lymphocytic Leukemia

Acute lymphocytic leukemia (ALL) can cause many different signs and symptoms. Most of these occur in all kinds of ALL, but some are more common with certain subtypes.

### Problems caused by low blood cell counts

Most signs and symptoms of ALL result from shortages of normal blood cells, which happen when the leukemia cells crowd out the normal blood-making cells in the bone marrow. These shortages show up on blood tests, but they can also cause symptoms, including:

- Feeling tired

- Feeling weak
- Feeling dizzy or lightheaded
- Shortness of breath
- Fever
- Infections that don't go away or keep coming back
- Bruising easily
- Bleeding, such as frequent or severe nosebleeds and bleeding gums

## **General symptoms**

Patients with ALL also often have several non-specific symptoms. These can include:

- Weight loss
- Fever
- Night sweats
- Fatigue
- Loss of appetite

Of course, these are not just symptoms of ALL and are more often caused by something other than leukemia.

## **Swelling in the abdomen**

Leukemia cells may build up in the liver and spleen, causing them to enlarge. This might be noticed as a fullness or swelling of the belly or feeling full after eating only a small amount. The lower ribs usually cover these organs, but when they are enlarged the doctor can feel them.

## **Enlarged lymph nodes**

ALL that has spread to lymph nodes close to the surface of the body (such as on the sides of the neck, in the groin, or in underarm areas), might be noticed as lumps under the skin. Lymph nodes inside the chest or abdomen may also swell, but these can be detected only by imaging tests such as CT or MRI scans.

## **Bone or joint pain**

Sometimes leukemia cells build up near the surface of the bone or inside the joint and cause bone or joint pain.

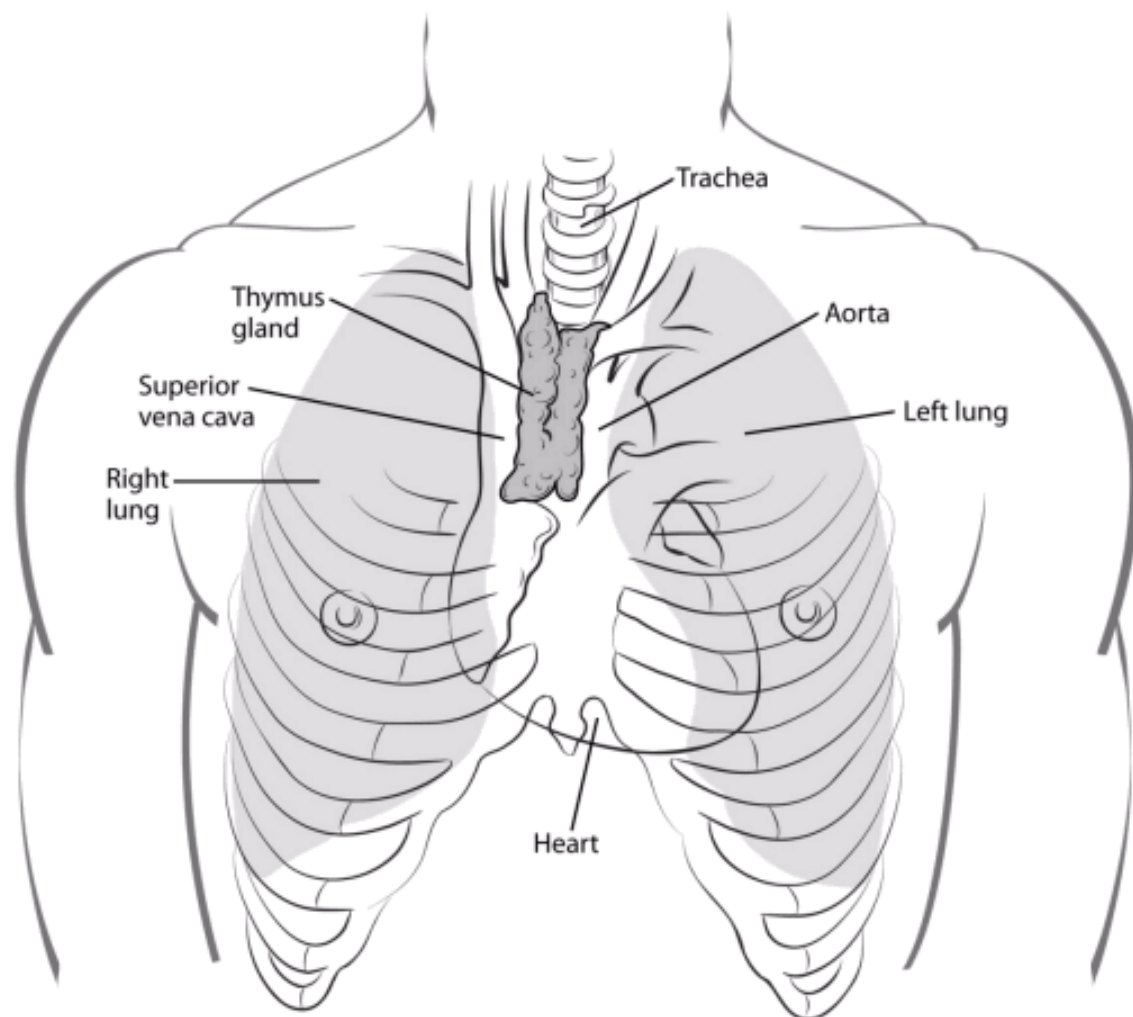
## **Spread to other organs**

Less often, ALL spreads to other organs:

- If ALL spreads to the brain and spinal cord it can cause headaches, weakness, seizures, vomiting, trouble with balance, facial numbness, or blurred vision.
- ALL may spread to the chest cavity, where it can cause fluid buildup and trouble breathing.
- Rarely, ALL may spread to the skin, eyes, testicles, kidneys, or other organs.

## **Symptoms from an enlarged thymus**

The T-cell subtype of ALL often affects the thymus, which is a small organ in the middle of the chest behind the sternum (breastbone) and in front of the trachea (windpipe). An enlarged thymus can press on the trachea, causing coughing or trouble breathing.



The superior vena cava (SVC), a large vein that carries blood from the head and arms back to the heart, passes next to the thymus. If the thymus is enlarged, it may press on the SVC, causing the blood to “back up” in the veins. This is known as *SVC syndrome*. It can cause swelling in the face, neck, arms, and upper chest (sometimes with a bluish-red color). It can also cause headaches, dizziness, and a change in consciousness if it affects the brain. The SVC syndrome can be life-threatening, and needs to be treated right away.

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# How Is Acute Lymphocytic Leukemia Diagnosed?

Certain [signs and symptoms](#) can suggest that a person might have acute lymphocytic leukemia, but tests are needed to confirm the diagnosis.

## Medical history and physical exam

If you have signs and symptoms that suggest you might have leukemia, the doctor will want to get a thorough medical history, including how long you have had symptoms and if you have any history of exposure to [risk factors](#).

During the physical exam, the doctor will probably focus on any enlarged lymph nodes, areas of bleeding or bruising, or possible signs of infection. The eyes, mouth, and skin will be looked at carefully, and a thorough nervous system exam may be done. Your abdomen will be felt for signs of an enlarged spleen or liver.

Your doctor may also order tests of your blood cell counts. If the results suggest leukemia, the doctor may refer you to a *hematologist*, a doctor who specializes in treating blood disorders (including blood cancers like leukemia). This doctor may run one or more of the tests described below.

## Tests used to diagnose and classify ALL

If your doctor thinks you have leukemia, he or she will need to check samples of cells from your blood and bone marrow to be sure of the diagnosis. Other tissue and cell samples may also be taken to help guide treatment.

### Blood tests

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

**Complete blood count (CBC) and blood cell exam (peripheral blood smear):** The complete blood count (CBC) measures the numbers of red blood cells, white blood cells, and platelets. This test is often done along with a differential (or diff) which looks at the numbers of the different types of white blood cells. These tests are often the first ones done on patients with a suspected blood problem.

For the *peripheral blood smear* (sometimes just called a smear), a drop of blood is smeared across a slide and then looked at under a microscope to see how the cells look. Changes in the numbers and the appearance of the cells often help diagnose leukemia.

Most patients with ALL have too many immature white cells in their blood, and not enough red blood cells or platelets. Many of the white blood cells will be lymphoblasts (blasts), which are immature lymphocytes not normally found in the bloodstream. Lymphoblasts do not function like normal, mature white blood cells.

Even though these findings may suggest leukemia, the disease usually is not diagnosed without looking at a sample of bone marrow cells.

**Blood chemistry and coagulation tests:** Blood chemistry tests measure the amounts of certain chemicals in the blood, but they are not used to diagnose leukemia. In patients already known to have ALL, these tests can help detect liver or kidney problems caused by spreading leukemia cells or 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 coagulation tests may also be done to make sure the blood is clotting properly.

## **Bone marrow tests**

**Bone marrow aspiration and biopsy:** Bone marrow samples are obtained by bone marrow aspiration and biopsy – tests 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 skin over the hip, the doctor numbs the skin and the surface of the bone by injecting a 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. 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 is removed with a slightly larger needle that is twisted as it is pushed down into the bone. With local anesthetic, most patients just feel some pressure and tugging from the biopsy, but a few may feel a brief pain. Once the biopsy is done, pressure will be applied to the site to help prevent bleeding.

These bone marrow tests are used to help diagnose leukemia. They may also be done again later to tell if the leukemia is responding to treatment.

**Routine exams under a microscope:** The bone marrow is 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 whether the cells appear mature (look like normal blood cells), or immature (lacking features of normal blood cells). The most immature cells are called lymphoblasts (or blasts for short).

Determining what percentage of cells in the bone marrow are blasts is particularly important. A diagnosis of ALL generally requires that at least 20% to 30% of the cells in the bone marrow are blasts. Under normal circumstances, blasts are never more than 5% of bone marrow cells.

Sometimes just counting and looking at the cells doesn't provide a definite diagnosis, and other lab tests are needed.

**Cytochemistry:** In cytochemistry tests, cells are put on a slide and exposed to chemical stains (dyes) that react only with certain substances found in or on different kinds of 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. For instance, one stain will turn parts of acute myeloid leukemia (AML) cells black, but has no effect on ALL cells.

**Flow cytometry and immunohistochemistry:** These tests are used for *immunophenotyping* – classifying cells according to proteins on or in the cells. This kind of testing is very helpful in determining the exact type of leukemia present. For diagnosing leukemia, it is most often done on cells from bone marrow, but it can also be done on cells from the blood, lymph nodes, and other body fluids.



For both flow cytometry and immunohistochemistry, samples of cells are treated with antibodies that stick to certain proteins. For immunohistochemistry, the cells are examined under a microscope to see if the antibodies stuck to them and so they have those proteins, while for flow cytometry a special machine is used.

These tests are helpful in diagnosing leukemia and lymphoma. For ALL, they are most often used to help determine the exact subtype of ALL in someone already thought to have the disease based on looking at the blood and bone marrow under a microscope.

## **Chromosome testing**

Normal human cells contain 23 pairs of chromosomes (bundles of DNA). In some cases of leukemia, the cells have chromosome changes. Sometimes a piece of a chromosome is missing – called a deletion.

More often in ALL, 2 chromosomes swap some of their DNA, so that part of one chromosome becomes attached to part of a different chromosome. This is called a *translocation*. The most common chromosome change in adult ALL is a translocation between chromosomes 9 and 22 [often written t(9;22)], which results in a shortened chromosome 22 (called the *Philadelphia chromosome*). About 1 out of 4 adults with ALL have this abnormality in their leukemia cells. This change is especially important because it can be targeted with certain drugs.

Information about chromosome changes can be useful in predicting a person's outlook and response to treatment. For this reason, chromosome testing is a standard part of the work-up of ALL patients.

**Cytogenetics:** For this test, the cells are grown in lab dishes until they start dividing and the chromosomes can be seen under a microscope. Then the chromosomes are looked at under a microscope to detect any changes.

Because it takes time for the cells to start dividing, cytogenetic testing often takes about 2 to 3 weeks. It is often used to look at cells in the bone marrow, but it can also be used to look at cells from the blood. An advantage of cytogenetic testing is that it looks at all of the chromosomes, and the doctor doesn't have to know in advance what changes to test for.

Not all chromosome changes can be seen under a microscope. Other lab tests can often help find these changes.

**Fluorescent in situ hybridization (FISH):** This is another way to look at chromosomes

and genes. It uses special fluorescent dyes that only attach to specific genes or parts of particular chromosomes. FISH can find most chromosome changes (such as translocations) that are visible under a microscope in standard cytogenetic tests, as well as some changes too small to be seen with usual cytogenetic testing.

FISH can be used on regular blood or bone marrow samples. Because the cells don't have to be able to divide for this test, it can also be used to look at cells from other tissues, like lymph node samples. It is very accurate and can usually provide results within a couple of days. But because FISH only tests for certain gene changes (and doesn't look at the chromosomes overall), it is best for looking for the changes that are important based on the kind of leukemia a person has.

**Polymerase chain reaction (PCR):** This is a very sensitive DNA test that can also find certain gene changes too small to be seen with a microscope, even if very few leukemia cells are present in a sample. Like FISH, it is used to find particular gene changes and not to look at the chromosomes overall. For ALL, it is often used to look for the gene made by the Philadelphia chromosome.

If the leukemia cells have a particular gene (or chromosome) change, PCR can be used after treatment to try to find small numbers of leukemia cells that may not be visible with a microscope.

## **Lumbar puncture (spinal tap)**

ALL can spread to the area around the brain and spinal cord. To check for this spread, doctors remove a sample of the fluid from that area (cerebrospinal fluid or CSF) for testing.

You may lay on your side or sit up for this test. The doctor first numbs an area in the lower part of the back over the spine. A small, hollow needle is then placed between the bones of the spine and into the area around the spinal cord to collect some fluid.

A lumbar puncture can also be used to put chemotherapy drugs into the CSF to try to prevent or treat the spread of leukemia to the spinal cord and brain.

## **Lymph node biopsy**

Removing a lymph node or part of a lymph node is often done to help diagnose lymphomas, but is only rarely needed with leukemia because the diagnosis is usually made looking at blood and bone marrow.

In this procedure, a surgeon cuts through the skin to remove all or part of a lymph node. If the node is near the skin surface, this is a simple operation that can often be done with local anesthesia, but if the node is inside the chest or abdomen, general anesthesia is used to keep you asleep during the biopsy.

When the entire lymph node is removed, it is called an *excisional lymph node biopsy*. If only part of the lymph node is removed, it is called an *incisional lymph node biopsy*.

## Imaging tests

Imaging tests use x-rays, sound waves, magnetic fields, or radioactive particles to produce pictures of the inside of the body. Because leukemia does not usually form tumors, imaging tests aren't as useful as they are for other types of cancer.

Imaging tests might be done in people with ALL, but they are done more often to look for infections or other problems, rather than for the leukemia itself. In some cases they may be done to help determine the extent of the disease, if it is thought it may have spread beyond the bone marrow and blood.

### X-rays

Chest x-rays may be done if the doctor suspects a lung infection. They may also be done to look for enlarged lymph nodes in the chest.

### 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 ALL, but it may be done if your doctor suspects leukemia cells are growing in an organ, like your spleen.

Sometimes a test that combines the CT scan with a [PET \(positron emission tomography\) scan](#) (PET/CT scan) is done. This is not often needed for patients with ALL.

### Magnetic resonance imaging (MRI) scan

[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 be distressing to some people. Newer, more open MRI machines may be another option. The MRI machine makes loud buzzing and clicking noises that you may find disturbing. Some places provide headphones or earplugs to help block this noise out.

## Ultrasound

[Ultrasound](#) can be used to look at lymph nodes near the surface of the body or to look for enlarged organs inside your abdomen such as the kidneys, liver, and spleen.

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

## Gallium scan and bone scan

[Gallium and bone scans](#) are not often done for ALL, but they may be useful if you have bone pain that might be caused by either an infection or cancer in the bones.

- [References](#)

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# How Is Acute Lymphocytic Leukemia Classified?

Most types of cancers are assigned numbered stages to describe their extent in the

body, based on the size of the tumor and how far the cancer has spread.

Acute lymphocytic leukemia (ALL), on the other hand, does not usually form tumor masses. It generally affects all of the bone marrow in the body and, in many cases, might have spread to other organs, such as the liver, spleen, and lymph nodes. Therefore the outlook for the patient with ALL depends on other information, such as the subtype of ALL (determined by lab tests), the age of the patient, and other lab test results.

Different systems have been used to classify ALL into subtypes.

## **The French-American-British (FAB) classification**

In the 1970s, a group of French, American, and British (FAB) leukemia experts divided ALL into 3 subtypes (L1, L2, and L3), based on the way the leukemia cells looked under the microscope after routine staining. This system has largely been replaced, as newer lab tests now allow doctors to classify ALL more accurately.

## **Classification based on immunophenotype**

Doctors have found that cytogenetic tests, flow cytometry, and other lab tests provide more detailed information about the subtype of ALL and the patient's prognosis. These tests help divide ALL into groups based on the *immunophenotype* of the leukemia, which takes into account:

- The type of lymphocyte (B cell or T cell) the leukemia cells come from
- How mature these leukemia cells are

These groups have largely replaced the FAB classification. The subtypes of ALL are now named as follows:

### **B-cell ALL**

- Early pre-B ALL (also called pro-B ALL) – about 10% of cases
- Common ALL – about 50% of cases
- Pre-B ALL – about 10% of cases
- Mature B-cell ALL (Burkitt leukemia) – about 4% of cases

### **T-cell ALL**

- Pre-T ALL – about 5% to 10% of cases
- Mature T-cell ALL – about 15% to 20% of cases

The subtypes of ALL each carry a slightly different outlook (prognosis), but other factors (like gene changes in the leukemia cells) may also have an impact. Some of these prognostic factors are listed in the next section.

## **Mixed lineage acute leukemias**

In recent years, newer lab tests have shown that a small number of acute leukemias actually have both lymphocytic and myeloid features. Sometimes the leukemia cells have both myeloid and lymphocytic traits in the same cells. In other cases, a person may have some leukemia cells with myeloid features and others with lymphocytic features. These types of leukemias may be called *mixed lineage leukemia*, *ALL with myeloid markers* (My+ ALL), *AML with lymphoid markers*, or *biphenotypic acute leukemia* (BAL).

Most studies suggest these leukemias tend to have a poorer outlook than standard subtypes of ALL or AML. Not all doctors agree on the best way to treat them. Intensive treatment (such as a stem cell transplant) is often used when possible, as there is a high risk of recurrence after treatment.

## **Prognostic factors**

As leukemia treatment has improved over the years, research has focused on why some people have a better chance for cure than others. Differences in patients that affect response to treatment are called *prognostic factors*. They help doctors decide if people with a certain type of leukemia should get more or less treatment.

### **Age**

Younger patients tend to have a better prognosis than older patients. There is no set cutoff for this, but generally those younger than 50 do better than those in their 50s, while people in their 50s do better than those in their 60s or older.

### **Initial white blood cell count**

People with a lower WBC count (less than 30,000 for B-cell ALL and less than 100,000 for T-cell ALL) at the time of diagnosis tend to have a better prognosis.

## **ALL subtype**

In general, T-cell ALL has a better prognosis, while mature B-cell ALL (Burkitt leukemia) has a poorer prognosis. Other subtypes of B-cell ALL fall somewhere in between. It's important to note that this doesn't apply to all cases. For instance, some subtypes of T-cell ALL have a better outlook than others.

## **Chromosome abnormalities**

The presence of a translocation between chromosomes 4 and 11 in the leukemia cells predicts a poorer outlook, so does extra chromosome 8 or a missing chromosome 7. The presence of Philadelphia chromosome (a translocation between chromosomes 9 and 22) used to predict a poorer outlook, but not if modern [targeted therapy drugs](#) are used.

## **Response to chemotherapy**

Patients who go into a complete remission (no visible leukemia in the bone marrow – see below) within 4 to 5 weeks of starting treatment tend to have a better prognosis than those for whom this takes longer. Patients who don't achieve a complete remission at all have a poorer outlook. The prognostic value of minimal residual disease (described below) is still being studied.

## **Status of acute lymphocytic leukemia after treatment**

How well leukemia responds to treatment affects the patient's long-term chance for recovery.

### **Remission**

A remission (*complete remission*) is usually defined as having no evidence of leukemia after treatment. This means the bone marrow contains fewer than 5% blast cells, the blood cell counts are within normal limits, and there are no signs or symptoms of the disease. A *molecular complete remission* means no evidence of leukemia cells in the bone marrow is found, even when using very sensitive lab tests, such as polymerase chain reaction (PCR). Even when leukemia is in remission, this does not always mean that it has been cured.

### **Minimal residual disease**

Minimal residual disease (MRD) is a term used after treatment when leukemia cells can't be found in the bone marrow using standard lab tests (such as looking at cells under a microscope), but they can still be detected with more sensitive tests (such as flow cytometry or PCR). Patients with MRD after treatment are more likely to have the leukemia relapse (come back after treatment) and overall have a poorer outlook than those who achieve a complete remission. Doctors are looking to see if these patients could benefit from further or more intensive treatment.

### Active disease

Active disease means that either there is evidence that the leukemia is still present during treatment or that the disease has relapsed (come back) after treatment. For a patient to be in relapse, more than 5% of the bone marrow must be made up of blast cells.

- [References](#)

[See all references for Acute Lymphocytic Leukemia](#)

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## What Should You Ask Your Doctor About Acute Lymphocytic Leukemia?

It is important to have frank, honest 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 [kind of acute lymphocytic leukemia \(ALL\)](#) do I have?
- Do I have any [specific factors](#) that might affect my prognosis?
- Do I need to have other [tests](#) before we can decide on treatment?
- Are there other doctors I need to see?
- How much experience do you have treating this type of leukemia?
- Should I get a second opinion before starting treatment? Can you suggest



someone?

- How soon do we need to start treatment?
- What are my [treatment choices](#)?
- Which treatment do you recommend, and why?
- Should we consider a [stem cell transplant](#)? When?
- What are the risks and side effects to the treatments that you recommend?
- 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 my prognosis?
- What will we do if the treatment doesn't work or if the leukemia comes back?
- What type of [follow-up](#) will I need after treatment?

Be sure to write down any questions you have that are not on this list. For instance, you might want specific information about recovery times so that you can plan your work or activity schedule. Or you might want to ask about [clinical trials](#) for which you may qualify. Taking another person and/or a tape recorder to the appointment can be helpful.

- [References](#)

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