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# Acute Lymphocytic Leukemia Early Detection, Diagnosis, and Types

Know the signs and symptoms of acute lymphocytic leukemia. Find out how ALL is tested for, diagnosed, and classified.

## 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 \(ALL\) Be Found Early?](#)
- [Signs and Symptoms of Acute Lymphocytic Leukemia \(ALL\)](#)
- [Tests for Acute Lymphocytic Leukemia \(ALL\)](#)

## Types of ALL

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

- [Acute Lymphocytic Leukemia \(ALL\) Subtypes and Prognostic Factors](#)

## 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.

- [Questions to Ask About Acute Lymphocytic Leukemia \(ALL\)](#)

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# Can Acute Lymphocytic Leukemia (ALL) Be Found Early?

- [For people at increased risk of ALL](#)

For many types of cancers, finding the cancer early makes it easier to treat. The American Cancer Society recommends [screening tests for early detection of certain cancers](#)<sup>1</sup> 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.

## For people at increased risk of ALL

Some people are known to have [a higher risk](#) of ALL (or other leukemias) because of a genetic disorder such as Down syndrome, or because they were previously treated with certain chemotherapy drugs or radiation. 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 people.

## Hyperlinks

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Jain N, Gurbuxani S, Rhee C, Stock W. Chapter 65: Acute Lymphoblastic Leukemia in Adults. In: Hoffman R, Benz EJ, Silberstein LE, Heslop H, Weitz J, Anastasi J, eds.

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## **Signs and Symptoms of Acute Lymphocytic Leukemia (ALL)**

menstrual bleeding in women

## General symptoms

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

- Weight loss
- Fever
- Night sweats
- 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, making them larger. 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 the organs 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, which can lead to bone or joint pain.

## Spread to other organs

Less often, ALL spreads to other organs:

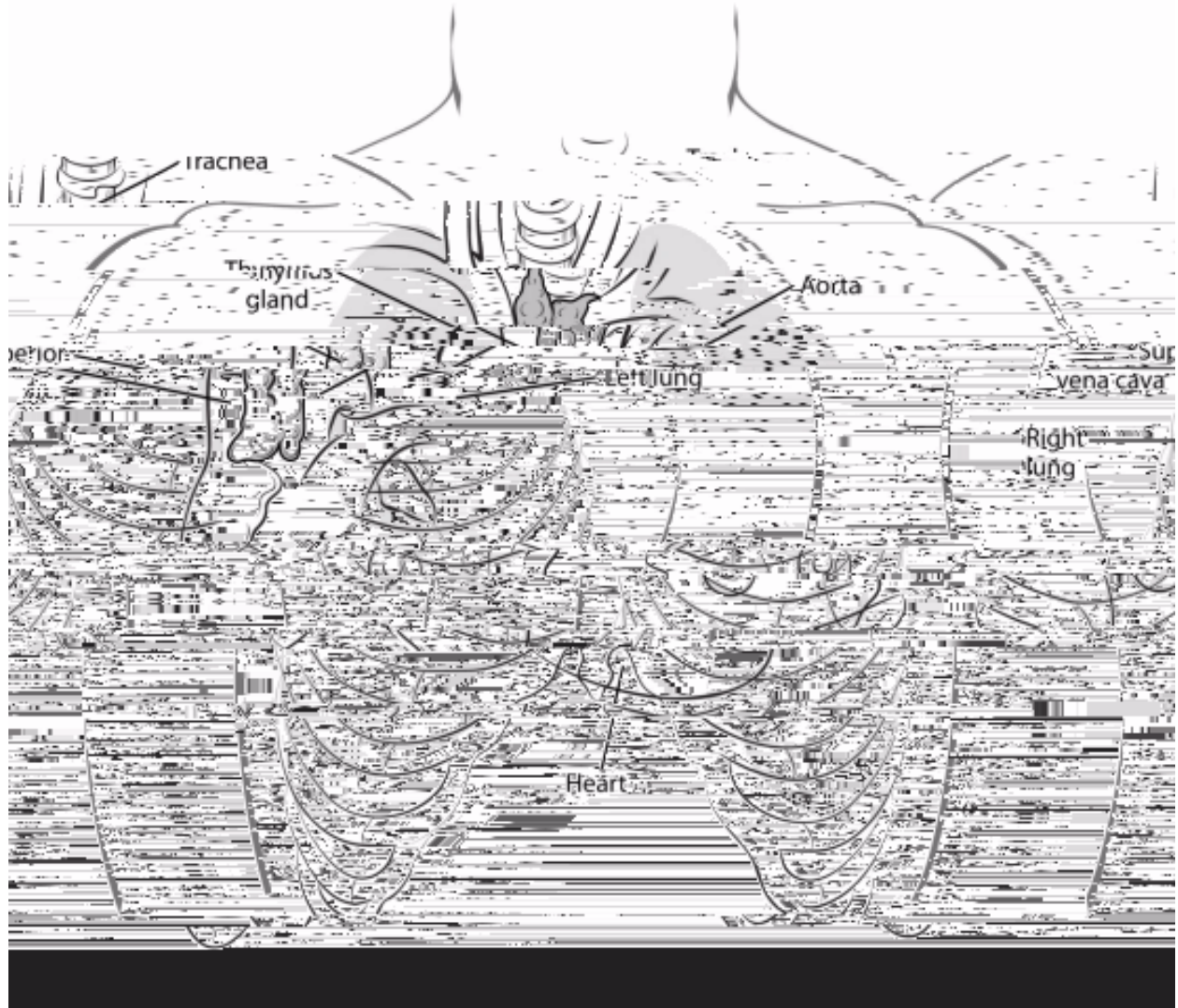
- If ALL spreads to the brain and spinal cord it can cause headaches, weakness,

seizures, vomiting, trouble with balance, facial muscle weakness or numbness, or blurred vision.

- ALL may spread inside the chest, where it can cause fluid buildup and trouble breathing.
- Rarely, ALL may spread to the skin, eyes, testicles, ovaries, 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, which can lead to 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)
- Headaches
- Dizziness
- Change in consciousness if it affects the brain

**The SVC syndrome can be life-threatening, and needs to be treated right away.**

## Hyperlinks

1. [www.cancer.org/cancer/types/acute-myeloid-leukemia/detection-diagnosis-staging/how-classified.html](http://www.cancer.org/cancer/types/acute-myeloid-leukemia/detection-diagnosis-staging/how-classified.html)
2. [www.cancer.org/cancer/types/acute-myeloid-leukemia/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/types/acute-myeloid-leukemia/detection-diagnosis-staging/how-diagnosed.html)

## References

Appelbaum FR. Chapter 98: Acute Leukemias in Adults. In: Niederhuber JE, Armitage JO, Dorshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 5th ed. Philadelphia, Pa. Elsevier: 2014.

Jain N, Gurbuxani S, Rhee C, Stock W. Chapter 65: Acute Lymphoblastic Leukemia in Adults. In: Hoffman R, Benz EJ, Silberstein LE, Heslop H, Weitz J, Anastasi J, eds. *Hematology: Basic Principles and Practice*. 6th ed. Philadelphia, Pa: Elsevier; 2013.

National Cancer Institute. Adult Acute Lymphoblastic Leukemia Treatment (PDQ®). Accessed at [www.cancer.gov/types/leukemia/patient/adult-all-treatment-pdq](http://www.cancer.gov/types/leukemia/patient/adult-all-treatment-pdq) on July 20, 2018.

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# Tests for Acute Lymphocytic Leukemia (ALL)

- [Medical history and physical exam](#)
- [Tests used to diagnose and classify ALL](#)
- [Imaging tests](#)

Certain signs and symptoms can suggest that a person might have acute lymphocytic leukemia (ALL), 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 possibly been exposed to anything considered a [risk factor](#).

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 spleen or liver enlargement.

If there is reason to think low levels of blood cells might be causing your symptoms (anemia, infections, bleeding or bruising, etc.), the doctor will most likely order blood tests to check your blood cell counts. You might also be referred to a **hematologist**, a doctor who specializes in diseases of the blood (including leukemia).

## Tests used to diagnose and classify ALL

If your doctor thinks you might have leukemia, they will need to check samples of cells from your blood and bone marrow to be sure. 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 peripheral blood smear:** The **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 called **lymphoblasts** (or just **blasts**) in their blood, and not enough red blood cells or platelets. Lymphoblasts are not normally found in the blood, and they don't 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 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.

**Coagulation tests:** Blood coagulation tests may be done to make sure the blood is clotting properly.

### **Bone marrow tests**

Leukemia starts in the bone marrow, so checking the bone marrow for leukemia cells is a key part of testing for it.

**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 pushed down into the bone. With local anesthetic, most patients just feel some pressure and tugging from the biopsy, but some 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.

### **Lab tests used to diagnose and classify ALL**

One or more of the following lab tests may be done on the samples to diagnose AML and/or to determine the specific [subtype of ALL](#)<sup>1</sup>.

**Routine exams with a microscope:** The bone marrow (and sometimes blood) samples are looked at with 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

marrow, but it can also be done on cells from the blood, lymph nodes, and other body fluids.

For ALL, these tests are most often used to help determine the exact subtype of in someone already thought to have ALL based on other tests.

### Chromosome tests

These tests look at the chromosomes (long strands of DNA) inside the cells. Normal human cells contain 23 pairs of chromosomes (bundles of DNA). In ALL, the cells sometimes have chromosome changes. Recognizing these changes can help identify certain types of ALL, and it can be important in determining a patient's outlook and likely response to some treatments. For this reason, chromosome testing is a standard part of the work-up for ALL.

The most common chromosome change in ALL is a **translocation**, in which, 2 chromosomes swap some of their DNA, so that part of one chromosome becomes attached to part of a different chromosome. The most common chromosome change in adult ALL is a translocation that 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<sup>2</sup>](#).

**Cytogenetics:** For this test, the cells are grown in lab dishes until they start dividing. 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.

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 and chromosome 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.

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.

### **Other molecular and genetic tests**

Other, newer types of lab tests can also be done on the samples to look for specific gene or other changes in the leukemia cells.

### **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**

A lymph node or part of a lymph node is often removed to help diagnose lymphomas, but this 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 just under the skin, 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 create pictures of the inside of the body. Leukemia does not usually form tumors, so imaging tests aren't as useful as they are for other types of cancer. Imaging tests might be done in people with ALL to help determine the extent of the disease, if it is thought to have spread beyond the bone marrow and blood. They might also be done to look for infections or other problems. .

### X-rays

Chest [x-rays](#)<sup>3</sup> 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](#)<sup>4</sup> uses x-rays to make detailed, cross-sectional images of your body.

This test can show 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.

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also be used to look at the testicles, if needed.

This is an easy test to have, and it uses no radiation.

## Hyperlinks

1. [www.cancer.org/cancer/types/acute-myeloid-leukemia/detection-diagnosis-staging/how-classified.html](http://www.cancer.org/cancer/types/acute-myeloid-leukemia/detection-diagnosis-staging/how-classified.html)
2. [www.cancer.org/cancer/types/acute-lymphocytic-leukemia/treating/targeted-therapy.html](http://www.cancer.org/cancer/types/acute-lymphocytic-leukemia/treating/targeted-therapy.html)
3. [www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/x-rays-and-other-radiographic-tests.html](http://www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/x-rays-and-other-radiographic-tests.html)

# Acute Lymphocytic Leukemia (ALL)

## Subtypes and Prognostic Factors

- [Subtypes of Acute Lymphocytic Leukemia \(ALL\)](#)
- [Prognostic factors for ALL](#)

For most types of cancer, determining the stage (extent) of the cancer is very important. The stage is based on the size of the tumor and how far the cancer has spread. This can be helpful in predicting a person's outlook and deciding on treatment.

Acute lymphocytic leukemia (ALL), on the other hand, does not usually form tumors. It generally affects all of the bone marrow in the body and, in some cases, has already spread to other organs, such as the liver, spleen, and lymph nodes, by the time it is found. Therefore ALL is not staged like most other cancers. The outlook for a person with ALL depends on other information, such as the subtype of ALL (determined by lab tests), the patient's age, and other lab test results.

### Subtypes of Acute Lymphocytic Leukemia (ALL)

Different systems have been used to classify ALL into subtypes.

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, known as the **FAB classification**, has largely been replaced, as [newer lab tests](#) now allow doctors to

- B-cell ALL with hypodiploidy (the leukemia cells have fewer than 44 chromosomes [normal cells have 46])
- B-cell ALL with hyperdiploidy (the leukemia cells have more than 50 chromosomes)
- B-cell ALL with a translocation between chromosomes 9 and 22 [t(9;22)] (the Philadelphia chromosome, which creates the *BCR-ABL1* fusion gene)
- B-cell ALL with a translocation between chromosome 11 and another chromosome
- B-cell ALL with a translocation between chromosomes 12 and 21 [t(12;21)]
- B-cell ALL with a translocation between chromosomes 1 and 19 [t(1;19)]
- B-cell ALL with a translocation between chromosomes 5 and 14 [t(5;14)]
- B-cell ALL with amplification (too many copies) of a portion of chromosome 21 (iAMP21)\*
- B-cell ALL with translocations involving certain tyrosine kinases or cytokine receptors (also known as “BCR-ABL1–like ALL”)\*

### **B-cell ALL, not otherwise specified**

### **T-cell ALL**

- Early T-cell precursor lymphoblastic leukemia\*

\* It's not yet clear if there's enough evidence that it's a unique group (meaning it is still a "provisional entity")

### **Mixed lineage acute leukemias**

A small number of acute leukemias 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, acute undifferentiated leukemia**, or, or **mixed phenotype acute leukemia (MPAL)**.

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 for ALL**





## 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 presence of minimal residual disease (described below) after initial treatment also seems to affect prognosis, although this is still being studied.

## Status of ALL during and 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 **complete molecular remission** means there is no evidence of leukemia cells in the bone marrow, 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 studying 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.

## Hyperlinks

1. [www.cancer.org/cancer/types/acute-myeloid-leukemia/causes-risks-prevention/what-causes.html](http://www.cancer.org/cancer/types/acute-myeloid-leukemia/causes-risks-prevention/what-causes.html)
2. [www.cancer.org/cancer/types/acute-lymphocytic-leukemia/treating/targeted-therapy.html](http://www.cancer.org/cancer/types/acute-lymphocytic-leukemia/treating/targeted-therapy.html)

## References

Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. 2016;127(20):2391-2405.

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Last Revised: October 17, 2018

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# Questions to Ask About Acute Lymphocytic Leukemia (ALL)

- [When you're told you have ALL](#)
- [When deciding on a treatment plan](#)
- [During and after treatment](#)



- How will we know if the treatment is working?
- What type of [follow-up](#)<sup>6</sup> will I need after treatment?
- 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 you on nights, holidays, or weekends?
- Do I need to change what I eat during treatment?
- Are there any limits on what I can do?
- Should I exercise? What should I do, and how often?
- Can you suggest a mental health professional I can see if I start to feel overwhelmed, depressed, or distressed?
- What would my options be if the treatment isn't working?
- Where can I find more information and support?

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](#)<sup>7</sup>

