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

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 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


References


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Signs and Symptoms of Acute Lymphocytic Leukemia (ALL)

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 of ALL.\(^1\)

**Symptoms caused by low numbers of blood cells**

Most signs and symptoms of ALL are the result of 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
- Pale skin
- Infections that don’t go away or keep coming back
- Bruises (or small red or purple spots) on the skin
- Bleeding, such as frequent or severe nosebleeds, bleeding gums, or heavy 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


References


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Tests for Acute Lymphocytic Leukemia (ALL)

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, he or she 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\(^1\).

**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 samples to classify them into specific types.

A key factor is whether the cells look mature (like normal blood cells), or immature (lacking features of normal blood cells). The most immature cells are called lymphoblasts (or just blasts).

Determining what percentage of cells in the bone marrow are blasts is particularly important. A diagnosis of ALL generally requires that at least 20% of the cells in the bone marrow are blasts. Under normal circumstances, blasts don’t make up 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 some types of leukemia cells. These stains cause color changes that can be seen under a microscope, which can help the doctor determine what types of cells are present. 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:** For both flow cytometry and immunohistochemistry, samples of cells are treated with antibodies, which are proteins that stick only to certain other proteins on cells. For immunohistochemistry, the cells are examined under a microscope to see if the antibodies stuck to them (meaning they have those proteins), while for flow cytometry a special machine is used.

These tests are used for immunophenotyping – classifying leukemia cells according to proteins on or in the cells. This kind of testing is very helpful in determining the exact type of leukemia. 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 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.

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 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 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.

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 make detailed images of the body using radio waves and strong magnets instead of x-rays. They are very helpful in looking at the brain and spinal cord. This test might be done if a lumbar puncture finds leukemia cells in the CSF, or if a person is having symptoms that could mean the ALL has spread to the area around the brain.

**Ultrasound**

Ultrasound can be used to look at lymph nodes near the surface of the body or to look for enlarged organs inside the abdomen such as the kidneys, liver, and spleen. It can also be used to look at the testicles, if needed.

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

**Hyperlinks**

Acute Lymphocytic Leukemia (ALL) Subtypes and Prognostic Factors

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.

References


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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 classify ALL more accurately.

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 gene and chromosome changes in the leukemia cells.

The World Health Organization (WHO) system, most recently updated in 2016, includes some of these factors to try to better classify ALL. The WHO system divides ALL into several groups:

**B-cell ALL**

**B-cell ALL with certain genetic abnormalities**¹ (gene or chromosome changes)

- 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 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

As leukemia treatment has improved over the years, research has focused on why some people have a better chance for cure than others. Different factors that affect a person’s prognosis (outlook) are called prognostic factors. They can help doctors decide if people with a certain type of leukemia should get more or less treatment.

Age

Among adults, 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.
Some of this might be because older patients are more likely to have unfavorable chromosome abnormalities (see below). Older patients are also more likely to have other medical conditions that can make it harder to treat them with more intense chemotherapy regimens.

**Initial white blood cell (WBC) count**

People with a lower WBC count (less than 30,000 for B-cell ALL and less than 100,000 for T-cell ALL) when they are first diagnosed tend to have a better prognosis.

**Gene or chromosome abnormalities**

Whether the leukemia cells have certain changes in their genes or chromosomes can affect prognosis. For example, patients tend to have a poorer outcome if the leukemia cells have:

- The Philadelphia chromosome (a translocation between chromosomes 9 and 22), although this outlook has improved with modern targeted therapy drugs
- A translocation between chromosomes 4 and 11
- A translocation involving chromosome 14
- Amplification (too many copies) of part of chromosome 21
- Fewer than 44 chromosomes (hypodiploidy)
- 5 or more chromosome changes (complex karyotype)

On the other hand, people tend to have a better outlook if the leukemia cells have:

- A translocation between chromosomes 12 and 21
- More than 50 chromosomes (hyperdiploidy)

**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

Questions to Ask About Acute Lymphocytic Leukemia (ALL)

It's important to have open and honest discussions with your cancer care team about your acute lymphocytic leukemia (ALL). Ask about anything you don’t understand or want to know more about. For instance, consider these questions:

When you're told you have ALL

- Can you explain to me what ALL is? How is it different from other types of leukemia?
- What type of ALL¹ do I have? What does this mean?
- Are there any other factors that might affect my prognosis²?
- Do I need any other tests before we can decide on treatment?
- Do I need to see any other types of doctors?
When deciding on a treatment plan

- How much experience do you and this medical center have treating this type of leukemia?
- What are my treatment choices?  
- Which treatment do you recommend, and why?
- Should we consider a stem cell transplant? When?
- Should I get a second opinion before starting treatment? Can you suggest a doctor or medical center?
- How soon do we need to start treatment?
- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?
- What are the risks and side effects to the treatments that you recommend?
- How will treatment affect my daily activities?
- What is my prognosis (outlook)?

During and after 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?
- What type of follow-up 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\(^7\) for which you may qualify.

Keep in mind, too, that doctors aren’t the only ones who can give you information. Other health care professionals, such as nurses and social workers, might be able to answer some of your questions. You can find out more about speaking with your health care team in The Doctor-Patient Relationship\(^8\).

Hyperlinks


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