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# About Acute Lymphocytic Leukemia (ALL)

## Overview of ALL

If you have been diagnosed with acute lymphocytic leukemia or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- [What Is Acute Lymphocytic Leukemia \(ALL\)?](#)

## Research and Statistics

See the latest estimates for new cases of acute lymphocytic leukemia and deaths in the US and what research is currently being done.

- [Key Statistics for Acute Lymphocytic Leukemia \(ALL\)](#)
- [What's New in Acute Lymphocytic Leukemia \(ALL\) Research?](#)

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# What Is Acute Lymphocytic Leukemia (ALL)?

Cancer starts when cells in the body begin to grow out of control. There are many kinds of cancer. Cells in nearly any part of the body can become cancer. To learn more about cancer and how it starts and spreads, see [What Is Cancer?](#)<sup>1</sup>

**Leukemias** are cancers that start in cells that would normally develop into different types of blood cells. Most often, leukemia starts in early forms of white blood cells, but some leukemias start in other blood cell types.

There are several types of leukemia, which are divided based mainly on whether the leukemia is acute (fast growing) or chronic (slower growing), and whether it starts in myeloid cells or lymphoid cells. Knowing the specific type of leukemia helps doctors better predict each person's prognosis (outlook) and select the best treatment.

**Acute lymphocytic leukemia (ALL)** is also called **acute lymphoblastic leukemia**. "Acute" means that the leukemia can progress quickly, and if not treated, would probably be fatal within a few months. "Lymphocytic" means it develops from early (immature) forms of **lymphocytes**, a type of white blood cell.

ALL starts in the bone marrow (the soft inner part of certain bones, where new blood cells are made). Most often, the leukemia cells invade the blood fairly quickly. They can also sometimes spread to other parts of the body, including the lymph nodes, liver, spleen, central nervous system (brain and spinal cord), and testicles (in males). Some cancers can also start in these organs and then spread to the bone marrow, but these cancers are not leukemia.

Other types of cancer that start in lymphocytes are known as **lymphomas** (either [non-Hodgkin lymphoma](#)<sup>2</sup> or [Hodgkin lymphoma](#)<sup>3</sup>). While leukemias like ALL mainly affect the bone marrow and the blood, lymphomas mainly affect the lymph nodes or other organs (but may also involve the bone marrow). Sometimes it can be hard to tell if a cancer of lymphocytes is a leukemia or a lymphoma. Usually, if at least 20% of the bone marrow is made up of cancerous lymphocytes (called lymphoblasts, or just **blasts**), the disease is considered leukemia.

## Normal bone marrow, blood, and lymph tissue

To understand leukemia, it helps to know about the blood and lymph systems.

### Bone marrow

Bone marrow is the soft inner part of certain bones. It is made up of blood-forming cells, fat cells, and supporting tissues. A small fraction of the blood-forming cells are **blood stem cells**.

Inside the bone marrow, blood stem cells go through a series of changes to make new blood cells. During this process, the cells develop into 1 of the 3 main types of blood cell

components:

- Red blood cells
- Platelets
- White blood cells

## Red blood cells

Red blood cells (RBCs) carry oxygen from the lungs to all other tissues in the body, and take carbon dioxide back to the lungs to be removed.

## Platelets

Platelets are actually cell fragments made by a type of bone marrow cell called a *megakaryocyte*. Platelets are important in plugging up holes in blood vessels caused by cuts or bruises.

## White blood cells

White blood cells (WBCs) help the body fight infections. The main types of WBCs include lymphocytes, granulocytes, and monocytes.

**Lymphocytes** are the main cells that make up lymph tissue, a major part of the immune system. Lymph tissue is found in lymph nodes, the thymus, the spleen, the tonsils and adenoids, and is scattered throughout the digestive and respiratory systems and the bone marrow.

Lymphocytes develop from cells called lymphoblasts to become mature, infection-fighting cells. There are 2 main types of lymphocytes:

- **B lymphocytes (B cells):** B cells help protect the body by making proteins called antibodies. The antibodies attach to germs (bacteria, viruses, and fungi) in the body, which helps the immune system destroy them.
- **T lymphocytes (T cells):** There are several types of T cells, each with a special job. Some T cells can destroy germs directly, while others play a role in either boosting or slowing the activity of other immune system cells.

ALL develops from early forms of lymphocytes. It can start in either early B cells or T cells at different stages of maturity. This is discussed in [Acute Lymphocytic Leukemia](#)

## [\(ALL\) Subtypes and Prognostic Factors<sup>4</sup>](#).

**Granulocytes** are WBCs that have granules in them, which are spots that can be seen under the microscope. These granules contain enzymes and other substances that can destroy germs, such as bacteria. The 3 types of granulocytes – neutrophils, basophils, and eosinophils – are distinguished by the size and color of their granules.

**Monocytes** also help protect the body against bacteria. After circulating in the bloodstream for about a day, monocytes enter body tissues to become macrophages, which can destroy some germs by surrounding and digesting them.

## Hyperlinks

1. [www.cancer.org/cancer/cancer-basics/what-is-cancer.html](http://www.cancer.org/cancer/cancer-basics/what-is-cancer.html)
2. [www.cancer.org/cancer/non-hodgkin-lymphoma.html](http://www.cancer.org/cancer/non-hodgkin-lymphoma.html)
3. [www.cancer.org/cancer/hodgkin-lymphoma.html](http://www.cancer.org/cancer/hodgkin-lymphoma.html)
4. [www.cancer.org/cancer/acute-lymphocytic-leukemia/detection-diagnosis-staging/how-classified.html](http://www.cancer.org/cancer/acute-lymphocytic-leukemia/detection-diagnosis-staging/how-classified.html)

## References

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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. *Hematology: Basic Principles and Practice*. 6th ed. Philadelphia, Pa: Elsevier; 2013.

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# Key Statistics for Acute Lymphocytic Leukemia (ALL)

The American Cancer Society's estimates for acute lymphocytic leukemia (ALL) in the United States for 2021 (including both children and adults) are:

- About 5,690 new cases of ALL (3,000 in males and 2,690 in females)
- About 1,580 deaths from ALL (900 in males and 680 in females)

The risk for developing ALL is highest in children younger than 5 years of age. The risk then declines slowly until the mid-20s, and begins to rise again slowly after age 50. Overall, about 4 of every 10 cases of ALL are in adults.

ALL is not a common cancer, accounting for less than half of 1% of all cancers in the United States. The average person's lifetime risk of getting ALL is about 1 in 1,000. The risk is slightly higher in males than in females, and higher in whites than in African Americans.

Most cases of ALL occur in children, but most deaths from ALL (about 4 out of 5) occur in adults. Children may do better than adults because of differences in the nature of childhood and adult ALL, differences in treatment (children's bodies can often handle aggressive treatment better than adult's), or some combination of these.

Visit the American Cancer Society's Cancer [Statistics Center](#)<sup>1</sup> for more key statistics.

## Hyperlinks

1. [www.cancer.org/research/cancer-facts-statistics.html](http://www.cancer.org/research/cancer-facts-statistics.html)

## References

American Cancer Society. *Cancer Facts & Figures 2021*. Atlanta, Ga: American Cancer Society; 2021.

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## What's New in Acute Lymphocytic Leukemia (ALL) Research?

Researchers are now studying the causes, genetics, and treatment of acute lymphocytic leukemia (ALL) at many medical centers, universities, and other institutions around the world.

### Genetics of ALL

Scientists are making great progress in understanding how changes in the DNA (genes) inside normal bone marrow cells can cause them to develop into leukemia cells. A greater understanding of the gene changes that often occur in ALL cells is providing insight into why these cells become abnormal. As researchers have found more of these changes, it is becoming clear that there are many types of ALL. Each of these might have different gene changes that affect how the leukemia will progress and which treatments might be most helpful. Doctors are now learning how to use these changes to help determine a person's outlook and whether they should receive more or less intensive treatment.

Perhaps even more important, this knowledge is now being used to help develop newer targeted therapy drugs against ALL. For example, targeted drugs such as imatinib (Gleevec) and dasatinib (Sprycel) are now used in treating ALL patients whose leukemia cells have the Philadelphia chromosome, and many other drugs targeting changes in ALL cells are now being developed.

Newer lab techniques are now helping researchers to identify and classify different types of ALL. Instead of looking at single genes, these tests can look at the patterns of many different genes in the cancer cells at the same time. This may add to the information that comes from the current lab tests.

This information may eventually allow more personalized treatment of ALL.

## Finding minimal residual disease

Recently, highly sensitive tests have been developed to detect even the smallest amount of leukemia left after treatment (known as minimal residual disease, or MRD), even when there are so few leukemia cells left that they can't be found by routine bone marrow tests.

For example, the polymerase chain reaction (PCR) test can identify even very small numbers of ALL cells in a sample, based on their gene changes. A PCR test can be useful in determining how completely the treatment has destroyed the ALL cells.

Doctors are now trying to determine what effect MRD has on a patient's outlook, and how this might affect the need for further or more intensive treatment.

## Improving treatment

Treatment for ALL can be very effective for some people, but it doesn't cure everyone (especially among adults), and it can often cause serious or even life-threatening side effects. Many studies are being done to find more effective and safer treatments for ALL.

### Chemotherapy

[Chemotherapy](#)<sup>1</sup> (chemo) is still the main treatment for nearly all cases of ALL. Studies are now being done to find the most effective combination of chemo drugs while limiting unwanted side effects. This is especially important in older patients, who often have a harder time tolerating current treatments.

New chemo drugs are also being developed and tested. For example, **clofarabine (Clolar)** is approved to treat childhood ALL and shows promise in early studies of adults with this disease. **Nelarabine (Arranon)** is a newer drug that can be used to treat T-cell ALL. Many other new drugs are also being studied.

Studies are also under way to determine whether patients with certain [prognostic factors](#)<sup>2</sup> might benefit from more intensive chemo, and whether some ALL patients might not need as much treatment.

Sometimes, chemo might not work as well because the leukemia cells become resistant to it. Researchers are now looking at ways to prevent or reverse this resistance by using other drugs along with chemotherapy.

## Stem cell transplants

Researchers continue to refine [stem cell transplants](#)<sup>3</sup> to try to increase their effectiveness, reduce complications and determine which patients are likely to be helped by this type of treatment. Many studies are being done to try to help determine exactly when allogeneic, autologous, and mini-transplants might best be used.

Doctors are also studying **donor leukocyte infusion (DLI)** in people who have already received an allogeneic transplant and who relapse. In this technique, the patient gets an infusion of white blood cells (leukocytes) from the same donor who contributed the stem cells for the original transplant. The hope is that the cells will boost the new immune system and add to the graft-versus-leukemia effect. Early study results have been promising, but more research on this approach is needed.

## Targeted therapy drugs

Newer [targeted drugs](#)<sup>4</sup> that specifically attack some of the gene changes seen in ALL cells are now becoming an important part of treatment for some people with ALL. These drugs work differently from standard chemotherapy drugs.

Many other drugs targeting other changes in ALL cells are now being studied as well. Examples include:

- **Proteasome inhibitors**, such as bortezomib (Velcade), carfilzomib (Kyprolis), and ixazomib (Ninlaro)
- **BCL-2 inhibitors**, such as venetoclax (Venclexta)
- **Syk inhibitors**, such as entospletinib
- **TORC1/2 inhibitors**, such as sapanisertib

## Immunotherapy

The goal of immunotherapy is to boost the body's immune system to help fight off or destroy cancer cells.

### ***Monoclonal antibodies***

These drugs are man-made versions of immune system proteins (antibodies). They can be developed to attach only to certain proteins, such as those that are found on ALL cells.

Some monoclonal antibodies are [already approved to treat ALL](#)<sup>5</sup>. These drugs are typically used if other treatments are no longer working, but they are now being studied for use earlier in the course of treatment as well (together with chemo).

Other monoclonal antibodies, such as **rituximab (Rituxan)** and **ofatumumab (Arzerra)**, are already used to treat other blood disorders, and are now being studied for use against ALL.

**Epratuzumab**, a newer antibody, has also shown promise against ALL in early studies. Further studies are under way.

One promising treatment approach is to attach a chemo drug to a monoclonal antibody (known as an **antibody-drug conjugate**, or ADC). The antibody serves as a homing device to bring the chemo drug to the leukemia cell. Several such drugs have shown promise in early studies, and are now being tested in larger clinical trials.

Several other monoclonal antibodies to treat ALL are now being studied as well.

### ***CAR T-cell therapy***

This is a promising new way to get the immune system to fight leukemia. For this technique, immune cells called **T cells** are removed from the patient's blood and altered in the lab so they have specific substances (called chimeric antigen receptors, or CARs) that will help them attach to leukemia cells. The [CAR T cells](#)<sup>6</sup> are then grown in the lab and infused back into the patient's blood, where they can now seek out the leukemia cells and attack them.

This technique has shown very promising results in early clinical trials against some types of advanced, hard-to-treat leukemias, and is now an option for some children and young adults with ALL. It is now being tested in older adults, too. With this treatment, some people have had very serious side effects, including very high fevers and dangerously low blood pressure in the days after it's given. Doctors are learning how to manage these side effects.

### ***Immune checkpoint inhibitors***

An important part of the immune system is its ability to keep itself from attacking other normal cells in the body. To do this, it uses "checkpoints" – molecules on immune cells that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to avoid being attacked by the immune system. But [newer drugs that target these checkpoints](#)<sup>7</sup> hold a lot of promise as treatments. Some of these drugs

are already being used to treat other types of cancer, and they are now being studied for use in ALL as well.

## Hyperlinks

1. [www.cancer.org/cancer/acute-lymphocytic-leukemia/treating/chemotherapy.html](http://www.cancer.org/cancer/acute-lymphocytic-leukemia/treating/chemotherapy.html)
2. [www.cancer.org/cancer/acute-lymphocytic-leukemia/detection-diagnosis-staging/how-classified.html](http://www.cancer.org/cancer/acute-lymphocytic-leukemia/detection-diagnosis-staging/how-classified.html)
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4. [www.cancer.org/cancer/acute-lymphocytic-leukemia/treating/targeted-therapy.html](http://www.cancer.org/cancer/acute-lymphocytic-leukemia/treating/targeted-therapy.html)
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7. [www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/immune-checkpoint-inhibitors.html](http://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy/immune-checkpoint-inhibitors.html)

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