Leukemia--Acute Lymphocytic

WHAT IS LEUKEMIA - ACUTE LYMPHOCYTIC (ALL) IN ADULTS?

What is acute lymphocytic leukemia?

Acute lymphocytic leukemia (ALL), also called *acute lymphoblastic leukemia*, is a cancer that starts from the early version of white blood cells called *lymphocytes* in the bone marrow (the soft inner part of the bones, where new blood cells are made).

Leukemia cells usually invade the blood fairly quickly. They can then spread to other parts of the body, including the lymph nodes, liver, spleen, central nervous system (brain and spinal cord), and testicles (in males). Other types of cancer also can start in these organs and then spread to the bone marrow, but these cancers are not leukemia.

The term “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. This is different from acute myeloid leukemia (AML), which develops in other blood cell types found in the bone marrow. For more information on AML, see our document *Leukemia--Acute Myeloid*.

Other types of cancer that start in lymphocytes are known as *lymphomas* (non-Hodgkin lymphoma or Hodgkin disease). The main difference between these types of cancers is that leukemias like ALL mainly affects the bone marrow and the blood, and may spread to other places, while lymphomas mainly affect the lymph nodes or other organs but may involve the bone marrow. Sometimes cancerous lymphocytes are found in both the bone marrow and lymph nodes when the cancer is first diagnosed, which can make it hard to tell if the cancer is leukemia or lymphoma. If more than 25% of the bone marrow is replaced by cancerous lymphocytes, the disease is usually considered leukemia. The size of lymph nodes is also important. The bigger they are, the more likely the disease will be considered a lymphoma. For more information on lymphomas, see our documents *Non-Hodgkin Lymphoma* and*Hodgkin Disease*.

There are actually many types of leukemia. They differ based on what types of cells they start in, how quickly they grow, which people they affect, and how they are treated. To understand leukemia, it helps to know about the blood and lymph systems.

Normal bone marrow, blood, and lymphoid tissue

Bone marrow

Bone marrow is the soft inner part of some bones, such as the skull, shoulder blades, ribs, pelvis, and bones in the spine. The bone marrow is made up of a small number of blood stem cells, more mature blood-forming cells, fat cells, and supporting tissues that help cells grow.

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 (which include lymphocytes, granulocytes, and monocytes)

Red blood cells

Red blood cells 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 help the body fight infections.

Lymphocytes

These are the main cells that make up lymphoid tissue, a major part of the immune system. Lymphoid 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. The 2 main types of lymphocytes are B lymphocytes (B cells) and T lymphocytes (T cells).

- **B lymphocytes:** B lymphocytes protect the body from invading germs by maturing into plasma cells, which make proteins called antibodies. The antibodies attach to the germs (bacteria, viruses, and fungi), which helps the immune system destroy them.
- **T lymphocytes:** 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.

Acute lymphocytic leukemia 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 the section "How is acute lymphocytic leukemia classified?"

Granulocytes

These are white blood cells 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

These white blood cells, which are related to granulocytes, 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.

Development of leukemia

Any type of early blood-forming cell of the bone marrow can turn into a leukemia cell. Once this change happens, the leukemia cells will not mature normally. The leukemia cells could reproduce quickly, and might not die when they should. Instead they survive and build up in the bone marrow. Over time, these cells spill into the bloodstream and spread to other organs, where they can keep other cells from functioning normally.

Types of leukemia

There are 4 main types of leukemia:

- Acute myeloid (or myelogenous) leukemia (AML)
- Chronic myeloid (or myelogenous) leukemia (CML)
- Acute lymphocytic (or lymphoblastic) leukemia (ALL)
- Chronic lymphocytic leukemia (CLL)

Acute leukemia versus chronic leukemia

The first factor in classifying leukemia is whether most of the abnormal cells are mature (look like normal white blood cells) or immature (look more like stem cells).

Acute leukemia: In acute leukemia, the bone marrow cells cannot mature properly. Immature leukemia cells continue to reproduce and build up. Without treatment, most people with acute leukemia would live only a few months. Some types of acute leukemia respond well to treatment, and many patients can be cured. Other types of acute leukemia have a less favorable outlook.

Chronic leukemia: In chronic leukemia, the cells can mature partly but not completely. These cells may look fairly normal, but they generally do not fight infection as well as normal white blood cells do. They also live longer, build up, and crowd out normal cells. Chronic leukemias tend to progress over a longer period of time, and most people can live for many years. But chronic leukemias are generally harder to cure than acute leukemias.

Myeloid leukemia versus lymphocytic leukemia

The second factor in classifying leukemia is the type of bone marrow cells that are affected.

Myeloid leukemia: Leukemias that start in early forms of myeloid cells – the cells that make white blood cells (other than lymphocytes), red blood cells, or platelet-making cells (megakaryocytes) – are *myeloid* leukemias (also known as *myelocytic, myelogenous, or non-lymphocytic* leukemias).

Lymphocytic leukemia: Leukemias that start in immature forms of lymphocytes are called *lymphocytic* leukemias (also known as *lymphoid* or *lymphoblastic* leukemias).

The rest of this document focuses on acute lymphocytic leukemia (ALL) in adults. For information on ALL in children, please see our document *Childhood Leukemia*. Chronic leukemias and acute myeloid leukemia of adults are discussed in other American Cancer Society documents.

CAUSES, RISK FACTORS, AND PREVENTION

What are the risk factors for acute lymphocytic leukemia?

A risk factor is something that affects your chance of getting a disease such as cancer. Some risk factors, like smoking, can be controlled. Others, like a person's age or family history, can't be changed.

But risk factors don't tell us everything. Having a risk factor, or even several risk factors, does not mean that you will definitely get the disease. And many people who get the disease may have few or no known risk factors. Even if a person has one or more risk factors and develops cancer, it is often very hard to know how much they might have contributed to the cancer.

There are only a few known risk factors for acute lymphocytic leukemia (ALL).

Radiation exposure

Being exposed to high levels of radiation is a risk factor for both ALL and acute myeloid leukemia (AML). Japanese atomic bomb survivors had a greatly increased risk of developing acute leukemia, usually within 6 to 8 years after exposure.

Treating cancer with radiation therapy also increases the risk of leukemia, although AML is more often seen than ALL. The risk seems to be higher if chemotherapy and radiation are both used in treatment.

The possible risks of leukemia from being exposed to lower levels of radiation, such as from medical imaging tests (such as x-rays) are not well-known. Exposure of a fetus to radiation within the first months of development may carry an increased risk of leukemia, but the extent of the risk is not clear.

If there is an increased risk from lower levels of radiation it is likely to be small, but to be safe, most doctors try to limit a person's exposure to radiation as much as possible.

Certain chemical exposures

The risk of ALL may be increased by exposure to certain chemotherapy drugs and certain chemicals, includingbenzene. Benzene is a solvent used in the rubber industry, oil refineries, chemical plants, shoe manufacturing, and gasoline-related industries, and is also present in cigarette smoke, as well as some glues, cleaning products, detergents, art supplies, and paint strippers. Chemical exposure is more strongly linked to an increased risk of AML than to ALL.

Certain viral infections

Infection with the human T-cell lymphoma/leukemia virus-1 (HTLV-1) can cause a rare type of T-cell acute lymphocytic leukemia. Most cases occur in Japan and the Caribbean area. This disease is not common in the United States.

In Africa, the Epstein-Barr virus (EBV) has been linked to Burkitt lymphoma, as well as to a form of acute lymphocytic leukemia. In the United States, EBV most often causes infectious mononucleosis ("mono").

Inherited syndromes

Acute lymphocytic leukemia does not appear to be an inherited disease. It does not seem to run in families, so a person's risk is not increased if a family member has the disease. But there are some inherited syndromes with genetic changes that seem to raise the risk of ALL. These include:

- Down syndrome
- Klinefelter syndrome
- Fanconi anemia
- Bloom syndrome
- Ataxia-telangiectasia
- Neurofibromatosis

Race/ethnicity

Acute lymphocytic leukemia is more common in whites than in African Americans, but the reasons for this are not clear.

Gender

Acute lymphocytic leukemia is slightly more common in males than in females. The reason for this is unknown.

Having an identical twin with ALL

Someone who has an identical twin who develops ALL in the first year of life has an increased risk of getting ALL.

Uncertain, unproven or controversial risk factors

Other factors that have been studied for a possible link to ALL include:

- Exposure to electromagnetic fields (such as living near power lines or using cell phones)
- Workplace exposure to diesel, gasoline, pesticides, and certain other chemicals
- Smoking
- Exposure to hair dyes

So far, none of these factors has been linked conclusively to ALL. Research in these areas continues.

EARLY DETECTION, DIAGNOSIS, AND STAGING

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 the section "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.

TREATING LEUKEMIA - ACUTE LYMPHOCYTIC (ALL) IN ADULTS

How is acute lymphocytic leukemia treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

General treatment information

Adult acute lymphocytic leukemia (ALL) is not a single disease. It is really a group of related diseases, and patients with different subtypes of ALL may have different outlooks and responses to treatment.

After your cancer is diagnosed and staged, your cancer care team will discuss your treatment options with you. Choosing a treatment plan is an important decision, so it is important to take time and think about your choices. Treatment options for each patient are based on the leukemia subtype as well as certain prognostic features (described in "How is acute lymphocytic leukemia classified?").

The main types of treatment used for ALL are:

- Chemotherapy
- Targeted therapy
- Stem cell transplant

Other treatments such as surgery, radiation therapy, or monoclonal antibodies, may be used in special circumstances.

Treatment of ALL typically lasts for about 2 years. It is often intense, especially in the first few months of treatment, so it is important that you are treated in a center that has experience with this disease.

You may have different types of doctors on your treatment team. The doctor in charge or your team will most likely be a hematologist, a doctor who specializes in treating blood diseases, including leukemia. Many other specialists may be involved in your care as well, including nurse practitioners, nurses, nutrition specialists, social workers, and other health professionals.

It is important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. It's also very important to ask questions if there is anything you're not sure about. You can find some good questions to ask in the section "What should you ask your doctor about acute lymphocytic leukemia?"

Treatment for ALL usually needs to start very soon after it is diagnosed, but if time permits, it is often a good idea to seek a second opinion. A second opinion might give you more information and help you feel confident about your chosen treatment plan.

The next few sections describe the types of treatments used for ALL. This is followed by a discussion of the typical treatment approach for ALL in adults.

TALKING WITH YOUR DOCTOR

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 aboutclinical trials for which you may qualify. Taking another person and/or a tape recorder to the appointment can be helpful.

AFTER TREATMENT

What happens after treatment for acute lymphocytic leukemia?

For some people with acute lymphocytic leukemia (ALL), treatment may get rid of the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about the leukemia coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are living full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence*, gives more detailed information on this.

For some people, the leukemia may not go away completely. These people may get regular treatments withchemotherapy, radiation therapy, or other therapies to help keep the leukemia in check for as long as possible. Learning to live with cancer that does not go away can be difficult and very stressful. It has its own type of uncertainty. Our document *When Cancer Doesn't Go Away*, talks more about this.

Follow-up care

Treatment for ALL typically lasts for years. If you have completed treatment, your doctors will still want to watch you closely. It's very important to go to all of your follow-up appointments. During these visits, your doctors will ask questions about any problems you may have and might do exams and lab tests or imaging tests to look for signs of leukemia or treatment side effects. Almost any cancer treatment can have side effects. Some may last for a few weeks to months, but others can last the rest of your life. This is the time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have.

It's also important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen.

If a relapse occurs, it is usually while the patient is being treated or shortly after they have finished chemotherapy. If this happens, treatment would be as described in the section "What if the leukemia doesn't respond or comes back after treatment?" It is unusual for ALL to return if there are still no signs of the disease within 5 years after treatment.

For more general information on dealing with a recurrence, you may also want to see the American Cancer Society document *When Your Cancer Comes Back: Cancer Recurrence*.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know all the details of your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- If you had surgery, a copy of your operative report(s)
- If you stayed in the hospital, a copy of the discharge summary that doctors prepare when patients are sent home
- If you had radiation therapy, a copy of your treatment summary
- If you had chemotherapy or other medicines (like targeted therapy), a list of your drugs, drug doses, and when you took them

The doctor may want copies of this information for his records, but always keep copies for yourself.

WHAT`S NEW IN LEUKEMIA - ACUTE LYMPHOCYTIC (ALL) IN ADULTS RESEARCH?

What's new in acute lymphocytic leukemia research and treatment?

Researchers are now studying the causes, diagnosis, supportive care, and treatment of acute lymphocytic leukemia (ALL) at many medical centers, university hospitals, and other institutions.

Genetics of leukemia

Scientists are making great progress in understanding how changes in a person's DNA can cause normal bone marrow cells to develop into leukemia cells. A greater understanding of the genes (regions of the DNA) involved in certain translocations that often occur in ALL is providing insight into why these cells become abnormal. Doctors are now looking to learn how to use these changes to help them determine a person's outlook and whether they should receive more or less intensive treatment.

As this information unfolds, it may also be used to develop newer targeted therapies against ALL. Drugs such asimatinib (Gleevec) and dasatinib (Sprycel) are examples of such treatments. They are now used in treating ALL patients whose leukemia cells have the Philadelphia chromosome.

Gene expression profiling

This new lab technique is being studied to help identify and classify different cancers. Instead of looking at single genes, this test uses a special technology to 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 by predicting which chemo drugs are likely to be most effective for each patient. These tests are also being used to find previously unknown changes inside ALL cells to help guide researchers in developing new drugs.

Detecting minimal residual disease

Progress in understanding DNA changes in ALL has already provided a highly sensitive test for detecting minimal residual disease after treatment – when so few leukemia cells are present that they cannot be found by routine bone marrow tests.

The polymerase chain reaction (PCR) test can identify ALL cells based on their gene translocations or rearrangements. This test can find one leukemia cell among many thousands of normal cells. A PCR test can be used in determining how completely chemotherapy has destroyed the ALL cells.

Doctors are now trying to determine if patients with minimal residual disease will benefit from further or more intensive treatment.

Improving chemotherapy

Studies are in progress to find the most effective combination of chemotherapy (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. Many other new drugs are also being studied.

Studies are also under way to determine whether patients with certain unfavorable prognostic features benefit from more intensive chemo, and whether some ALL patients with favorable prognostic factors might not need as much treatment.

The effectiveness of chemotherapy may be limited in some cases 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 to try to increase their effectiveness, reduce complications and determine which patients are likely to be helped by this 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* 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 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.

Monoclonal antibodies

These drugs are man-made versions of immune system proteins (antibodies). They can be targeted to attach only to certain molecules, such as proteins on the surface of certain lymphocytes.

Some monoclonal antibodies, such as rituximab (Rituxan) and alemtuzumab (Campath), are already used to treat other blood disorders and are now being studied for use against ALL. Early results have been favorable, but it is still too early to know for sure.

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

Another approach is to attach a chemo drug to a monoclonal antibody. The antibody serves as a homing device to bring the chemo drug to the cancer cell. One such drug, inotuzumab ozogamicin, has shown promise in treating ALL.

Studies of several other monoclonal antibodies to treat ALL are now under way as well.

Source: