All About Adult Acute Lymphocytic Leukemia (ALL)

This article is a more specific discussion of ALL. Please be sure to read Leukemia: The Basics first, so you have a basic understanding of leukemia.

ALL is also referred to as acute lymphoid leukemia and acute lymphoblastic leukemia.

What is ALL?

ALL is a blood cancer that affects the white blood cells. There are two main types of white blood cells, lymphocytes (affected by ALL) and myelocytes (affected by AML). Lymphocytes are further broken down into B and T cell lymphocytes. ALL is a spectrum of disease comprised of several different subtypes, named for the cell type that is affected (B or T) and how abnormal the cell appears under a microscope. A person with ALL develops abnormal numbers of white blood cells rather quickly, usually over weeks, giving the disease the name "acute".

The white blood cell (WBC) count may be higher or lower than normal, but the WBCs that are being produced are immature and do not function well. Because WBCs are an important part of fighting infections, patients often have multiple infections that don't respond to treatment before they are diagnosed. Some people will have low red blood cell or platelet counts because the overpopulation of WBCs crowds out these cells.

What causes ALL and am I at risk?

In most cases, the cause of ALL is unknown. There are some factors that are known to increase a person's risk of developing ALL, including previous treatment with chemotherapy or radiation therapy, exposure to large amounts of radiation (such as an atomic bomb), or the presence of a genetic disorder (including Down syndrome, Klinefelter's syndrome, neurofibromatosis, and Fanconi anemia). Research has identified viruses, such as Epstein-Barr, HTLV1, and HIV, as potential causes in some cases.

There are an estimated 5970 new cases of ALL diagnosed annually in the United States. ALL is the most common type of childhood cancer; nearly 56% of ALL cases occur in individuals less than 20 years old. ALL accounts for 0.4% of all adult cancer cases (and 20% of adult leukemia cases), but makes up 25% of all childhood cancers. ALL can occur at any age, but is most common in children, ages 2 to 4, and adults over age 50. This article will address ALL in adults. It impacts women and men equally and has a slightly higher incidence in Hispanics.

How can I prevent ALL?

In most ALL cases, we don’t know the cause of the diagnosis. Thus, there aren’t any ways to prevent ALL from developing. It is also important to exercise, don’t smoke, and maintain a nutritious diet to lower your risk of cancer in general.

What screening tests are used for ALL?

There are no standard screening tests used for ALL. Be sure to tell your health care providers of any history of being exposed to radiation (as in an atomic bomb detonation or nuclear accident), or if you have a genetic syndrome be sure to discuss your potential increased risk for developing ALL.

What are the signs of ALL?

In ALL, white blood cells do not fully mature and therefore cannot function properly. These immature cells, called "blasts", also suppress normal blood cells from forming, further compounding the problem. Symptoms are caused by the abnormal number of and malfunctioning of blood cells and/or these cells infiltrating organs. Symptoms can include weight loss, fever, infection, easy
bleeding or bruising, shortness of breath, or weakness. These symptoms can also be signs of common illnesses, like a cold or flu, and it is not uncommon for a person to be seen several times by a healthcare provider before receiving a diagnosis of ALL. Most infections are just infections and not leukemia, so treating a suspected infection is appropriate and this short delay in diagnosis is not likely to affect the course of the disease. What is important is that a person returns to their healthcare provider for further investigation if the symptoms they have do not respond to the prescribed treatment (often antibiotics). When blood counts are checked, abnormal counts of blasts are seen on the results. Once this occurs, further testing is required to clarify a diagnosis of leukemia and determine the type of ALL.

How is ALL diagnosed?

Once ALL is suspected, further blood tests, including a blood smear, and a bone marrow biopsy and aspiration may be performed to confirm and better classify the ALL. On a blood smear, blast cells are usually seen. A bone marrow biopsy confirms the diagnosis and allows the laboratory to determine the sub type. A lumbar puncture (spinal tap) is also done to evaluate if there are blast cells in the spinal fluid. You may also have tests to determine if there are chromosomal abnormalities (karyotyping or cytogenetic analysis). Other laboratory tests that may be performed include a FISH (fluorescence in situ hybridization) test and a PCR (polymerase chain reaction). Your cells will also be examined through a process called immunophenotyping which helps to determine what subtype of ALL you have.

ALL is classified using the World Health Organization system, which replaced the FAB (French American British) system in 2001. These classifications are made based on the chromosomal and genetic abnormalities present in the cells. They also guide the treatment of the disease. There are 3 basic categories: precursor B cell ALL, precursor T cell ALL, and mature B cell ALL (also called Burkitt lymphoma). You may hear your care team identify the leukemia by the chromosomal or genetic abnormalities, which are described below. The "t" stands for translocation and the p, q and v have to do with the location of the abnormality on the chromosome.

- B lymphoblastic leukemia/lymphoma with recurrent genetic abnormalities
  - B lymphoblastic leukemia/lymphoma with t(9;22)(q34;q11.2), BCR-ABL
  - B lymphoblastic leukemia/lymphoma with t(v;11q23); MLL rearranged
  - B lymphoblastic leukemia/lymphoma with t(12;21)(p13;q22) TEL-AML1 (ETV6-RUNX1)
  - B lymphoblastic leukemia/lymphoma with hyperdiploidy
  - B lymphoblastic leukemia/lymphoma with hypodiploidy
  - B lymphoblastic leukemia/lymphoma with t(5;14)(q31;q32) IL3-IGH
  - B lymphoblastic leukemia/lymphoma with t(1;19)(q23;p13.3) TCF3-PBX1

- T Cell lymphoblastic leukemia / lymphoma

How is ALL treated?

Chemotherapy for ALL is one of the most complex treatment plans used in any type of cancer. It is broken down into three phases, induction phase, consolidation (or intensification) phase and maintenance phase. The goal of therapy is to induce a remission, usually defined as less than 5% blast cells found in the bone marrow. Surgery is not used because ALL is a disease of the blood, which circulates throughout the whole body. This means an effective treatment must address disease throughout the body.

The selection of a chemotherapy regimen is dependent on age, as well as the sub-type of ALL. In particular, if the subtype is Philadelphia chromosome positive or negative (Ph+ or Ph-). The Philadelphia Chromosome is a genetic abnormality that was first identified in chronic myelogenous leukemia (CML), but is also seen in over 20% of adult ALL cases. (Read more about the Philadelphia Chromosome) Philadelphia Chromosome positive ALL (Ph+ ALL) had long carried the poorest prognosis of all ALL types, but the discovery of a class of medications that target this genetic abnormality has brought new hope for these patients. These medications are called tyrosine kinases inhibitors (TKIs). Unlike in CML treatment, TKI’s do not offer a potential cure for Ph+ ALL or effective long-term treatment, but it can induce a temporary remission, and in patients who receive an autologous stem cell transplant, the addition of a TKI improves overall survival. TKI’s used in the treatment of Ph+ ALL include imatinib, ponatinib, nilotinib, bosutinib, blinatumomab, and dasatinib. There are targeted therapies that may be used for relapsed or refractory Ph+ ALL including, blinatumomab and inotuzumab ozogamicin.
Induction therapy consists of a combination of several medications, most often a steroid (dexamethasone or prednisone), a chemotherapy called vincristine, an anthracycline (daunorubicin or doxorubicin) and an enzyme called asparaginase. This regimen is called hyper-CVAD.

Other chemotherapeutic medications may be used based on the subtype of ALL. These include nelarabine, pegaspargase, cytarabine, cyclophosphamide, methotrexate, and rituximab. Many patients will be treated as part of a clinical trial to allow researchers to better identify the best regimens.

Consolidation therapy uses some similar medications, but is more variable in its schedule, depending upon the particular subtype of ALL. Consolidation is given over a period of 4 to 8 months. If a patient was a candidate for stem cell transplant, then the transplant would likely be done in lieu of consolidation and maintenance therapy.

Maintenance therapy consists of mercaptopurine (6-MP), methotrexate, vincristine, and prednisone, given over a period of 2 to 3 years. Studies found no benefit to increasing this time, but did find outcomes to be worse if the maintenance period was shorter. Maintenance therapy is not given for Burkitt's lymphoma leukemia, as this subtype has a high cure rate with induction and consolidation therapy alone.

A new type of immunotherapy, called adoptive cell transfer (ACT) was approved. In this treatment, the patient’s own immune cells are used to treat their cancer. Tisagenlecleucel is a CAR-T immunotherapy that may be used in the treatment of both Ph+ and Ph- refractory ALL.

Because of potential risk to fertility associated with chemotherapy medications used to treat ALL, discuss fertility preservation options with your healthcare provider before starting treatment.

**Central nervous system (CNS) prophylaxis**

While less than 10% of patients have CNS involvement of leukemia (leukemia found in the spinal fluid) at the time of diagnosis, 50-75% of patients will develop this by 1 year if not given preventive therapy. The most effective therapy to prevent CNS disease in adults with ALL is intrathecal chemotherapy. This involves giving chemotherapy directly into the spinal canal. This can be achieved by lumbar puncture (spinal tap), or through a catheter called an Ommaya reservoir that is surgically implanted in the head. This catheter allows for multiple, repeat intrathecal infusions without needing multiple lumbar punctures. The number of intrathecal infusions given is dependent on the subtype of ALL and the risk of CNS disease associated with that subtype.

**Stem cell transplant**

The use of stem cell transplant for ALL is not completely clear. It is most often used early in therapy for patients with high-risk subtypes of ALL in first remission. Clinical trials are evaluating the optimal time for transplant (first or second remission, before maintenance therapy, etc.) and trying to determine which patients are best served with this modality.

**Complications & Concerns of Leukemia and Treatment**

People with leukemia are at risk of infection (due to few and poorly functioning white blood cells) and bleeding (due to low platelet counts) even before any therapy is started. Because these abnormalities are a result of the leukemia, it is necessary to treat the leukemia in order to correct the abnormal blood counts. Leukemia treatment causes the blood cell counts and function to temporarily get worse. During this time, patients will receive blood and platelet transfusions, antibiotics and take precautions to prevent infection and bleeding.

Hand washing is the single best way to prevent infection and should be performed frequently by patients, visitors, caregivers and healthcare personnel. Even the best hand washers get infections, so we implement a few other restrictions to help in the cause. People with leukemia may have restrictions on consuming some types of fresh fruit and vegetables or receiving fresh flowers or plants while in the hospital. (See the gift guide for ideas on what to send a patient with these restrictions) You may think this sounds odd, but these items can harbor bacteria and may put the patient at higher risk of infection. We ask people who are sick (or who have sick family members at home) not visit the patient in person and if they absolutely must, they need to wear a mask and wash their hands well.

In most cases, some type of infection or fever is inevitable. When this happens, the patient will typically have several tests done...
to look for a source of the infection, which can include blood, urine and stool cultures, and a chest x-ray. Antibiotics may be started, or adjusted if they are already being given. Many times the source of the infection is never identified and general antibiotics that treat a variety of things will be used. The patient will receive these antibiotics until their white blood count reaches a level that will allow them to fight the infection on their own.

Over the course of their treatment, patients will require either blood (for low hemoglobin levels) or platelet (for low platelet counts) transfusions. People with low hemoglobin counts (also called anemia) can experience fatigue, shortness of breath or appear pale. A low platelet count (also called thrombocytopenia) can lead to bleeding. This can be as small as gums bleeding when brushing the teeth or a nosebleed, to dangerous bleeding, such as a stroke. Patients should use caution to avoid bumping themselves with normal activities; they should not shave with a razor (electric razor is okay, with caution) and should avoid any activities that increase the risk of bleeding or bruising. Patients should always inform their healthcare team if they have symptoms of anemia or thrombocytopenia.

A diagnosis of leukemia is very scary, but understanding what is happening and what to expect can help alleviate some anxiety. Learning about the treatments, potential side effects and how the healthcare team will manage them can help patients and their caregivers, friends and family.

**Clinical Trials**

There are clinical research trials for most types of cancer, and every stage of the disease. Clinical trials are designed to determine the value of specific treatments. Trials are often designed to treat a certain stage of cancer, either as the first form of treatment offered, or as an option for treatment after other treatments have failed to work. They can be used to evaluate medications or treatments to prevent cancer, detect it earlier, or help manage side effects. Clinical trials are extremely important in furthering our knowledge of disease. It is through clinical trials that we know what we do today, and many exciting new therapies are currently being tested. Talk to your provider about participating in clinical trials in your area. You can also explore currently open clinical trials using the [OncoLink Clinical Trials Matching Service](http://www.frederickmd.org/oncolink/clinical_trials).

**Follow-up Care and Survivorship**

Once you have been treated for ALL, you will need to be closely followed by your oncology team. At first, you will have follow-up visits fairly often. For the first year you will have a physical exam, and CBC (lab draw) with differential monthly. Re-examinations of bone marrow aspirate, cerebrospinal fluid (CSF), and echocardiogram may be ordered based on your disease process, genetics, and treatment. This will be determined by your health care team. In the second year, you will have a physical exam and CBC with differential every 3 months. After 3 years, you will have physical exam and CBC with differential every 6 months, or as indicated by your health care providers. Depending upon your age at time of diagnosis you may also have regular testicular exams.

Fear of recurrence, relationship challenges, financial impact of cancer treatment, employment issues, and coping strategies are common emotional and practical issues experienced by ALL survivors. Your healthcare team can identify resources for support and management of these practical and emotional challenges faced during and after cancer.

Cancer survivorship is a relatively new focus of oncology care. With some 15 million cancer survivors in the US alone, there is a need to help patients transition from active treatment to survivorship. What happens next, how do you get back to normal, what should you know and do to live healthy going forward? A survivorship care plan can be a first step in educating yourself about navigating life after cancer and helping you communicate knowledgeably with your healthcare providers. Create a survivorship care plan today on [OncoLink](http://www.oncolink.org).

**Resources for More Information**

**Leukemia and Lymphoma Society**

Provides disease information and support resources.


**Leukemia Research Foundation**
Provides disease information and a glossary of medical terms related to leukemia.

http://www.leukemia-research.org

American Society of Hematology
The official website of doctors who treat blood disorders including leukemia.

http://www.hematology.org/Patients/Cancers/Leukemia.aspx

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