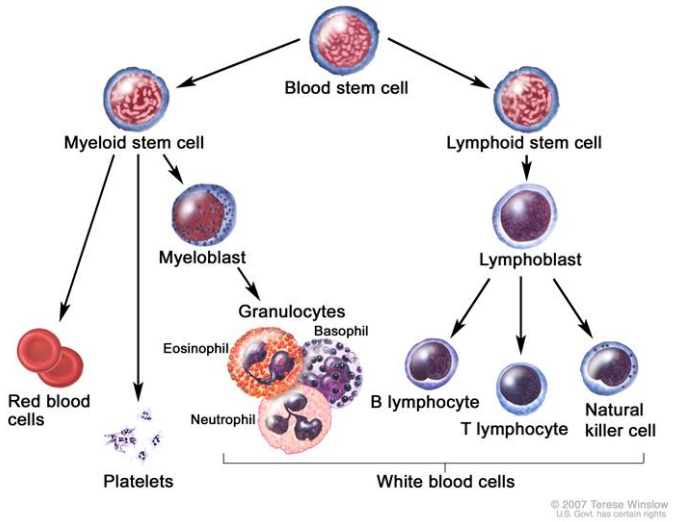
Qure
Center for Complete Care
Blood Diseases, Cancer, Stem Cell Transplantation

Childhood Acute Lymphoblastic Leukemia

What is acute lymphoblastic leukemia (ALL)?

ALL is a cancer of the blood in which the bone marrow makes too many immature lymphocytes (white blood cells). All blood is made in the bone marrow where blood cells come from stem cells. **Acute lymphoblastic leukemia** (ALL) is a cancer of the white blood cells, where too many immature abnormal white blood cells, called "blasts", are found in the bone marrow. Depending on which kind of lymphoblast is in excess it may be **pre-B cell leukemia**, or (more rarely) **T-cell leukemia**. These blasts crowd out the normal blood cells in the bone marrow and spread to the blood. They can also spread to the brain, spinal cord, and/or other organs of the body. Lymphoblasts do not work like normal lymphocytes and are not able to fight infection. As the number of leukemia cells increases in the blood and bone marrow, there is less room for healthy red blood cells, and platelets which may also lead to anemia, and easy bleeding.



What are signs of childhood ALL?

- Fever.
- Large mass in chest (T-cell only)
- Easy bruising/bleeding
- Bone or joint pain.
- Weakness, feeling tired, or looking pale.

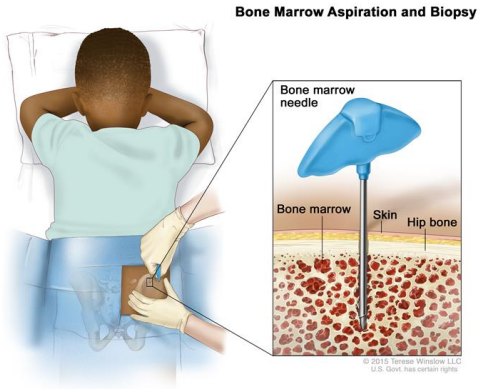
What causes ALL?

Nobody knows for sure, but commonly there is nothing in the environment or diet that caused this. It is typically not inherited so other children in the family should not be at risk and it is not infectious so it cannot be passed onto other children or playmates.

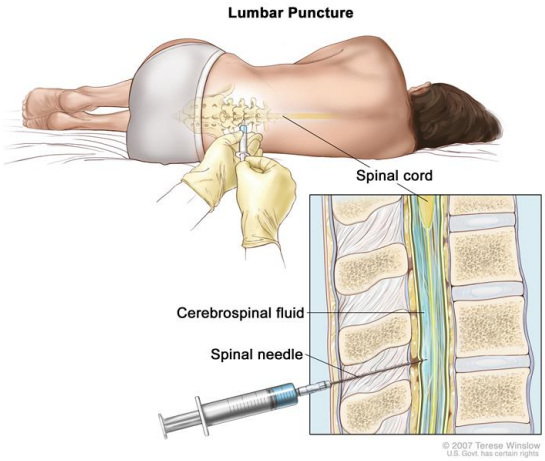
How is ALL diagnosed?

We may suspect the diagnosis from the blood count but the tests described below will confirm it and find out if leukemia has spread to other parts of the body e.g. spinal fluid

- **Physical exam and history:** An exam of the body to check or signs of disease, such as lumps or anything else that seems unusual e.g. testes enlargement.
- **Blood tests:** such as complete blood count (CBC) which tells the number and type of each blood cell, and blood chemistry studies because certain substances may be increased in acute leukemia.
- **Chest x-ray:** to see if leukemia cells have formed a mass in the middle of the chest.
- **Bone marrow aspiration and biopsy:** Removal of liquid bone marrow and a tiny piece of bone by inserting a needle into the hipbone while the child is sedated. A pathologist views the marrow sample under a microscope to look at the leukemia cells. Special tests done include flow cytometry to look at markers on the surface of the cells to confirm the diagnosis and subtype of ALL and genetic analysis of the leukemia cells.



- **Lumbar puncture:** The removal of a teaspoon of cerebrospinal fluid (CSF) by placing a needle between two bones in the lower spine while the child is sedated. CSF is reviewed under a microscope for leukemia, and chemotherapy is injected at the same time. This is repeated throughout the entire course of treatment so that leukemia cells don't hide there.



Qure
Center for Complete Care
Blood Diseases, Cancer, Stem Cell Transplantation

Is childhood ALL curable?

The treatment for T-cell and B-cell ALL is similar, and long-term cure rates with modern day **chemotherapy** are 80% or higher provided your child is in the correct risk group and receives up-to-date treatment. Cure rates vary depending on the risk factors described below and your doctor will be able to give you a better estimate after taking those all into account.

What are risk Groups in ALL?

Risk groups tell us how likely the ALL is to come back without adequate treatment and are used to plan chemotherapy. There are three risk groups in childhood ALL and the final risk group is determined by your doctor:

- **Standard (low) risk**: Includes children aged 1 to younger than 10 years who have a white blood cell count of less than 50,000/µL at the time of diagnosis.
- **High risk**: Includes children 10 years and older and/or children who have a white blood cell count of 50,000/µL or more at the time of diagnosis.
- **Very high risk:** Includes children younger than age 1, and children with certain changes in their leukemia genes or who have signs of leukemia after the first month of treatment.

This information includes a special bone marrow test done at the end of the first month of treatment (induction) known as **minimal residual disease** (**MRD) test.** It is common for T-ALL patients to have small amounts of MRD on their first test and to need another bone marrow MRD test after the next phase of treatment (consolidation).

What is chemotherapy?

Cancer fighting drugs (chemotherapy) are given as a combination. Chemotherapy is taken by mouth or injected into a vein or muscle to reach cancer cells throughout the body. Chemotherapy is also placed directly into the cerebrospinal fluid (**intrathecal**). In the initial stage of treatment called **Induction**, we administer chemotherapy to remove all visible signs of leukemia and allow normal blood cells to be restored, which is called *remission*. Your doctor will use information gathered at diagnosis and after the first month of treatment to give you your final risk group, and what further treatment your child should receive.

Does chemotherapy have side effects?

All people who receive cancer treatment are at risk of having side effects, some of which are mild but others of which can be life-threatening In addition to killing tumor cells, chemotherapy can damage normal tissue. Side effects usually get better when the medication is stopped but sometimes last a long time or never go away. Common side effects include nausea, vomiting, hair loss, low blood counts and fatigue (tiredness). Drugs are given to prevent nausea and vomiting. Hair loss is usually temporary but very rarely it may be permanent. Low blood counts may require transfusion or increase the risk of infection. Chemotherapy **side effects** are listed on the sheets your doctor will give you, these vary depending on the medication. It is important to remember that the treatment given is essential for cure and most patients will have very few of the side effects listed.

Qure
Center for Complete Care
Blood Diseases, Cancer, Stem Cell Transplantation

Why is ALL treatment so prolonged with so many different drugs?

When we check a bone marrow after induction, remission simply means we cannot see the leukemia cells we know to be present. If these are not treated adequately the ALL will come back (relapse) and the majority of patients who suffer a relapse will die. By giving different chemotherapy drugs in combination, in different "phases" listed below which last 1-2 months each (except maintenance which lasts 2-3 years), this increases the chances of killing all the leukemia cells and getting a long-term cure.

1) **Induction**
2) **Consolidation**
3) **Interim maintenance**
4) **Delayed intensification**
5) **Maintenance**

Does my child need to be in hospital the whole time?

No, at the start of treatment your child may need to be admitted **inpatient** to receive IV fluid, especially with a high white blood cell count which can cause complications. **High dose chemotherapy** is also usually given **inpatient** in the hospital. However, the majority of treatment is administered in an **outpatient clinic** or **day care unit.** After the first 7 months of intense treatment, your child is less likely to need admission to hospital for fever or low blood counts and with your doctor's permission can return to school.

What dietary and what other precautions should I take?

Chemotherapy suppresses your child's immune system so infections are a major concern. We place diet and activity restrictions for the first month of treatment, and often for the first 6-7 months, especially for young children. We prohibit any street/outside food and recommend home food be thoroughly cooked. No special foods will help with cure but we ban vitamin or nutritional supplements that might interfere with chemotherapy. Visits to movie theaters, malls, weddings, or other crowded places and plane, bus or railway travel are all banned. You should contact your doctor *immediately* if in spite of these precautions your child develops a fever >100.4F, diarrhea, cough, vomiting, abdominal pain, headaches or looks unwell.

Will my child need a bone marrow transplant (BMT)?

Children with high-risk or very high–risk ALL receive more treatment but only some patients in the very high risk group may need a bone marrow transplant (BMT). Your doctor will discuss with you if your child has risk factors that will make a BMT in his or her best interest.

Will my child need radiation?

Radiation is not routinely given unless there is evidence the ALL has spread to testes (in which case the testes will need to be radiated) or brain (in which case the head will need to be radiated). Your doctor will discuss with you if this is the case.

Qure
Center for Complete Care
Blood Diseases, Cancer, Stem Cell Transplantation

Sample protocol for Patient with ALL

Methods for Giving Chemotherapy

- **PO** - Drug is given by tablet or liquid swallowed through the mouth.
- **IV** - Drug is given using a needle or tubing inserted into a vein. Drugs can be given rapidly over a few minutes ("push") or slowly over minutes or hours ("infusion").
- **IM** - Drug is given into a muscle using a needle.
- **IT** - Drug used to treat the brain and spinal cord is given using a needle inserted through the back into the fluid surrounding the spinal cord.
- **SC** – Drug is given by subcutaneous injection

Standard Treatment Tables

Induction is to kill as many of the leukemia cells as possible so the disease goes into remission.

Drug	How drug will be given	Days
Cytarabine	IT	1 (or at diagnosis)
Vincristine	IV	1, 8, 15, and 22
Daunorubicin	IV	1, 8, 15, and 22
Dexamethasone **(< 10 years old)**	PO twice a day (may be given IV)	1 - 14
Prednisone **(≥ 10 years old)**	PO twice a day (may be given IV)	1 - 28
PEG-asparaginase	IV or IM	4
Methotrexate	IT	8, 15†, 22† and 29

†Subjects with leukemia in the CNS (CNS3) also get IT MTX on these days.

YOUR DOCTOR WILL NOT BE ABLE TO TELL YOU THE TREATMENT THAT FOLLOWS UNTIL THE RESULTS FROM THE BONE MARROW ASPIRATE MRD AFTER INDUCTION.

Consolidation is to kill remaining leukemia cells and lasts about 56 days (or about 8 weeks).

Drug	How the drug will be given	Days
Cyclophosphamide	IV over 30-60 minutes	1 and 29
Cytarabine	IV over 1-30 minutes or SC	1-4, 8-11, 29-32, and 36-39
Mercaptopurine	PO	1-14 and 29-42
Vincristine	IV	15, 22, 43 and 50
Pegaspargase*	IV or IM	15 and 43
Methotrexate	IT	1, 8, 15, and 22
Testicular Irradiation+		ONLY IF testicular disease

+Males with clinically evident or biopsy proven testicular disease.

Interim Maintenance is to kill remaining leukemia cells especially in spinal fluid and lasts 63 days (or about 9 weeks). You will have four 2-3 day long inpatient hospital stays.

Drug	How the drug will be given	Days
High Dose Methotrexate	IV over 24 hours†	1, 15, 29 and 43
Vincristine	IV	1, 15, 29,and 43
Mercaptopurine	PO	1 to 56
Methotrexate	IT	1 and 29

† Since methotrexate decreases folic acid, replacement with leucovorin will be given starting 42 hours after each dose.

Qure
Center for Complete Care
Blood Diseases, Cancer, Stem Cell Transplantation

Delayed Intensification repeats the treatment given in the first few months to eradicate leukemia cells and lasts about 56 days (or about 8 weeks)

Drug	How drug will be given	Days
Vincristine	IV	1, 8, 15, 43 and 50
Dexamethasone	PO (twice a day)	1-7 and 15-21
Doxorubicin	IV	1, 8, and 15
Pegaspargase	IV or IM	4 and 43
Cyclophosphamide	IV over 30-60 minutes	29
Cytarabine	IV over 1-30 minutes or SC	29-32, and 36-39
Thioguanine	PO	29-42
Methotrexate	IT	1, 29, and 36

Maintenance is to kill residual leukemia cells so the disease stays in remission. Maintenance cycles last 12 weeks and are repeated until 2 years from the start of Interim Maintenance for females and 3 years for males.

Drug	How drug will be given	Days
Vincristine	IV	Once every 4 weeks
Prednisone	PO (twice a day)	For 5 days every 4 weeks
Methotrexate	PO	Once a week
Mercaptopurine	PO	1-84
Methotrexate	IT	Once every 12 weeks*

*For the first 4 cycles (one year), patients get an extra dose on Day 29.