T-cell acute lymphoblastic leukaemia (T-cell ALL)

T-cell acute lymphoblastic leukaemia (T-cell ALL) is an acute leukaemia in which too many abnormal T-cells are produced in the bone marrow. T-cell ALL is an aggressive subtype of ALL. Find out what it is, the symptoms to look out for, how to diagnose it and treatment options.

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What is T-cell ALL?

T-ALL is an uncommon, aggressive sub-type of ALL. In T-cell ALL, too many T-cells are produced in the bone marrow. These T-cells are immature and abnormally shaped. They are called 'leukaemia cells' or 'blasts' and do not fight infections properly. These large numbers of T-cells prevent you making the other blood cells you need.

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What causes T-cell ALL?

The exact cause of T-cell ALL is unknown. However factors that put people at higher risk of leukaemia are thought to be changes in their chromosomes and genes.

- 60-80% of patients who develop T-cell ALL have abnormal changes in their chromosomes and genes. These are acquired mutations that cannot be passed on to your children.
- The remaining patients do not have any detectable chromosomes or mutations abnormalities.
- Of the patients who develop with T-cell ALL 15% are of children and 25% are adults. There is a peak incidence of T-cell ALL in children aged between about 2 to 5 years. T-cell ALL affects slightly more males than females at all ages.

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Genetic changes in T-cell ALL

Patients with T-cell ALL have the following acquired mutations that cannot be passed on to your children.

- Up to 80% of patients with T-ALL have a deletion of the *CDKN2A* gene.
- 60% of patients with T-ALL have deletions of *TAL1* (1p32) gene.
- The most common mutations occur in the *NOTCH1*/*FBXW7* pathway (60% of adult patients).
- Only two of these genes, *NOTCH1* and *CDKN2A*/*2B* are mutated in more than 50% of T-ALL cases, and a large variety of genes are mutated at lower frequency.

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Symptoms of T-cell ALL

At first, the symptoms of T-cell ALL are vague and can be mistaken for other illnesses. Sometimes, a routine blood test will show signs of ALL such as high levels of white blood cells. However, the majority of patients have symptoms at diagnosis.

Patients who have T-cell ALL produce large amounts of abnormal leukaemia T-cells. These leukaemia cells overwhelm the bone marrow preventing it from producing adequate numbers of red blood cells, platelets and white blood cells.

In T-cell ALL, patients can present with extremely high white blood cell counts. Involvement of the central nervous system (CNS) is also seen in 10% of patients at diagnosis.

Reduced levels of normal blood cells cause some of the main symptoms of ALL. The most common symptoms and signs of ALL are:

- Weakness or fatigue
- Pale skin
- Fever and/or night sweats
- Unexpected weight loss or anorexia
- Difficulty breathing
- Easy bruising, bleeding gums, purpura or petechiae
- Purpura (purple-coloured patches) but unlike bruises they are not due to injury
- Petechiae (flat, 2 mm, red/purple spots). They do not disappear when pressed beneath a glass

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We have more information about symptoms of leukaemia.

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How is T-cell ALL diagnosed?

To diagnose your T cell ALL, your haematology team will perform tests that include:

Full blood counts

A full blood count will:

- Measure the number of red cells, different types of white cells and platelets in your blood. High levels of T-cell white blood cell lymphocytes can determine a diagnosis of T-cell ALL.
- Abnormal-looking lymphocytes with an indistinct nucleus and reduced amount of cytoplasm can be demonstrated by examining under a microscope a small sample of the blood smeared onto a glass slide.

Bone marrow aspiration or biopsy

Bone marrow samples obtained by aspiration or a biopsy can be examined under a microscope to confirm a T-cell ALL diagnosis if it is not obvious from the blood sample.

Your haematologist will take your bone marrow sample from your hip bone. You should have a local anaesthetic and your haematologist will use a special biopsy needle. If you need more pain relief or have any concerns, make sure to raise this during the procedure.

Lumbar puncture

A lumbar puncture will reveal if leukaemia cells have entered your central nervous system. A member of your haematology team will insert a fine needle in the lumbar region of your lower back. This enables collection of a small amount of (CSF). At the same time you will nearly always have an injection of chemotherapy into the space around your spinal cord – this is called intrathecal chemotherapy. Your cerebrospinal fluid will be examined to see if there are any leukaemia cells present in it.

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Chromosome abnormalities or gene mutations tests

Patients with T-cell ALL have chromosome abnormalities and gene mutations. Tests for these abnormalities help your haematology team understand how your ALL might develop over time. This also helps them to organise your treatment plan.

They can be identified by specialist tests of blood or bone marrow samples.

Standard cytogenetic analysis

This involves examining in the laboratory leukaemia cells while they are dividing. This will indicate any chromosome abnormalities and gene mutations. Cytogenetic means study of chromosomes.

Molecular cytogenetic analysis

This method uses a technique called fluorescence in situ hybridisation which can characterise chromosome abnormalities. It labels small portions of DNA with fluorescent particles allowing your haematology team to:

- Detect sequences of DNA
- Locate a gene on a chromosome
- Determine the number of copies of a gene
- Detect any chromosomal abnormalities

Polymerase chain reaction (PCR) test

PCR tests analyse genetic information. PCR tests can detect evidence of the Philadelphia chromosome in particular. The Philadelphia chromosome is present in 20 to 30% of adults with ALL. PCR tests throughout your treatment period can check your response to current treatment too. Your haematology team will adjust your treatment according to your results.

Immunophenotyping

Immunophenotyping is a method to detect the proteins found on blood cells. Each type of blood cell has different proteins on its surface. Your haematology team can use immunophenotyping to tell which of your lymphocytes are affected by looking for the B-cell or T-cell proteins.

Flow cytometry

Flow cytometer measures the size and structures of thousands of cells or particles in a short amount of time. Particles or cells dissolved in a fluid float past at least one laser. Flow

cytometry is used to in identify various cell types only seen in certain diseases. One of the most common is in the diagnosis of blood related cancers such as leukaemia.

Imaging tests

Imaging tests that can help assess the impact of the leukaemia on the organs of your body include X-rays, ultrasounds, computer tomography (CT) scans and magnetic resonance imaging (MRI).

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Treatment of T-cell ALL

Your haematology team will start your ALL treatment soon after your diagnosis. This is because ALL has a fast progression. In general you will need to go to hospital and remain there for several weeks.

Your treatment is often discussed and decided upon at group meetings. These are called multi-disciplinary teams (MDTs). They include different types of doctors and nurses to make sure the treatment selected for you is the most appropriate.

Video: https://youtu.be/e8EpY-VJEI0

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Treatment phases

There are three separate individual phases included in the treatment of T-cell ALL. They include:

Induction treatment and CNS prophylaxis phase

Induction treatment is the first treatment given after diagnosis. The aim of the induction treatment is to kill as many leukaemia cells as possible. Induction treatment should encourage complete remission.

Induction treatment consists of a combination of chemotherapy drugs. Your haematology team will administer your treatment in hospital. You should be in hospital for up to eight weeks.

Induction treatment for ALL

Central nervous system prophylaxis and treatment

At diagnosis, leukaemia cells are present in the CSF of around 10% of patients. If not identified at diagnosis, they can contribute to the CNS relapse seen in 30% of cases. There is great variability in the presence of leukaemia cells in the CNS.

The majority of patients will need treatment with intrathecal chemotherapy. This is where chemotherapy is injected into the fluid around your spinal cord after a lumbar puncture. It can be given as treatment or prevention of leukaemia cells in the CNS disease. Oral or intravenous chemotherapy cannot be used instead as they do not penetrate into the CSF at high enough levels.

Consolidation treatment

Patients receive consolidation treatment to help them reinforce their remission. Consolidation treatment consists of lower doses of the drug combinations used for induction. Consolidation treatment reduces the risk of a relapse. A relapse is when a patient responds to treatment, but after six months, the response stops. This is also sometimes called a recurrence.

Consolidation therapy consists of lower doses of the drug combinations used for induction.

Consolidation treatment for ALL

Maintenance treatment

You should receive maintenance treatment after your consolidation treatment to prevent relapse of ALL. Without maintenance therapy, there is a significant risk that the ALL will return.

Maintenance treatment consists of low-dose combination chemotherapy. You can receive it as an outpatient. However you will need to attend hospital for intravenous and intrathecal chemotherapy, usually given as day cases. Maintenance treatment will last for two to three years.

Maintenance treatment for ALL

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Common treatment options

Chemotherapy

Patients with a new diagnosis of T-ALL should receive intensive chemotherapy. Your haematology team will administer this with or without cranial radiotherapy. A common combination of chemotherapies used for T-cell ALL is:

- Vincristine
- An anthracycline drug such as daunorubicin, doxorubicin or idarubicin
- A steroid such as dexamethasone or prednisolone

If your haematology team think it would help you, they will add other drugs such as:

- Cyclophosphamide or cytarabine
- Asparaginase or pegaspargase (a derived version of asparaginase)
- A tyrosine kinase inhibitor (TKI) for patients who have the Philadelphia chromosome.
    - TKIs are drugs that inhibit the tyrosine kinase enzyme that control the function of a cell. They stop the cell growing and dividing.
    - Imatinib is an effective TKI, although there are newer ones.

Nelarabine

Nelarabine is a water-soluble, anticancer drug, toxic to T-cell leukaemia cells. It is effective for the treatment of adults with refracted or relapsed ALL.

Stem cell transplant

A stem cell transplant works by replacing your stem cells in your bone marrow with healthy donor stem cells. The aim of replacing your stem cells is to help you only make normal blood cells again. Patients can also receive a stem cell transplant to reduce the risk of replace. There are two types of stem cell transplant:

- Allogeneic stem cell transplants are a stem cell transplants that use stem cells from a matching sibling or matching donor.
- Autologous stem cell transplants use stem cells from the patients themselves. They are rarely performed for ALL patients.

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Need support?

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Page last reviewed: 31 January 2023
Updated January 2026
Next review due: 30 June 2026

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