

Acute Lymphoblastic Leukaemia (ALL)

Acute lymphoblastic leukaemia is a cancer of blood forming cells in the bone marrow. Abnormal immature white blood cells (lymphoblasts) fill the bone marrow and spill into the bloodstream. Production of normal blood cells is affected causing anaemia, bleeding problems, and infections. There is a good chance of a cure with treatment.

What is leukaemia?

Leukaemia is a cancer of cells in the bone marrow (the cells which develop into blood cells).

Cancer is a disease of the cells in the body. There are many types of cancer which arise from different types of cell. What all cancers have in common is that the cancer cells are abnormal and do not respond to normal control mechanisms. Large numbers of cancer cells build up because they multiply 'out of control', or because they live much longer than normal cells, or both.

With leukaemia, the cancerous cells in the bone marrow spill out into the bloodstream. There are several types of leukaemia. Most types arise from cells which normally develop into white blood cells. (The word leukaemia comes from a greek word which means 'white blood'.) If you develop leukaemia it is important to know exactly what type it is. This is because the outlook (prognosis) and treatments vary for the different types. Before discussing the different types of leukaemia it may help to know some basics about normal blood cells and how they are made.

What is normal blood made up of?

- **Blood cells**, which can be seen under a microscope, make up about 40% of the blood's volume. Blood cells are divided into three main types:
 - **Red cells** (erythrocytes). These make blood a red colour. One drop of blood contains about five million red cells. Red cells contain a chemical called haemoglobin. This binds to oxygen, and takes oxygen from the lungs to all parts of the body.
 - **White cells** (leukocytes). There are different types of white cells which are called neutrophils (polymorphs), lymphocytes, eosinophils, monocytes, and basophils. They are part of the immune system. Their main role is to defend the body against infection.
 - **Platelets**. These are tiny and help the blood to clot if we cut ourselves.
- **Plasma** is the liquid part of blood and makes up about 60% of the blood's volume. Plasma is mainly made from water, but contains many different proteins and other chemicals such as hormones, antibodies, enzymes, glucose, fat particles, salts, etc.

When blood spills from your body (or a blood sample is taken into a plain glass tube) the cells and certain plasma proteins clump together to form a clot. The remaining clear fluid is called serum.

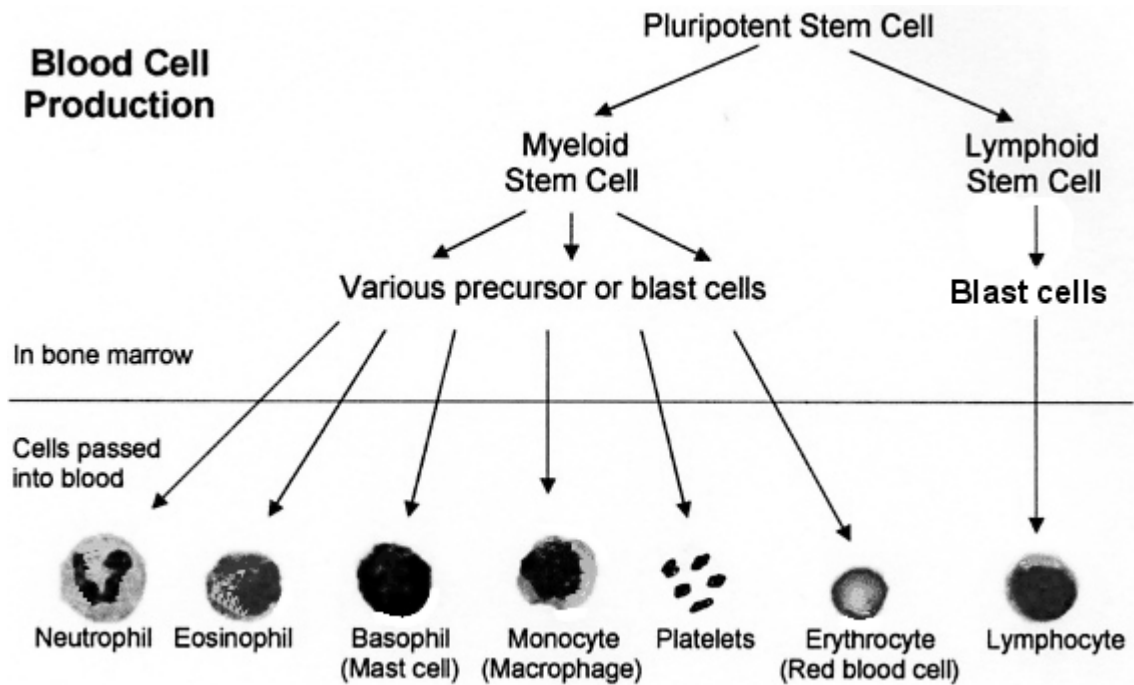
The bone marrow, stem cells and blood cell production

Bone marrow

Blood cells are made in the bone marrow by 'stem' cells. The bone marrow is the soft 'spongy' material in the centre of bones. The large flat bones such as the pelvis and breast-bone (sternum) contain the most bone marrow. To constantly make blood cells you need a healthy bone marrow. You also need nutrients from your diet including iron and certain vitamins.

Stem cells

Stem cells are primitive (immature) cells. There are two main types in the bone marrow - myeloid and lymphoid stem cells. These derive from even more primitive common 'pluripotent' stem cells. Stem cells constantly divide and produce new cells. Some new cells remain as stem cells and others go through a series of maturing stages ('precursor' or 'blast' cells) before forming into mature blood cells. Mature blood cells are released from the bone marrow into the bloodstream.



- Lymphocyte white blood cells develop from lymphoid stem cells. There are three types of mature lymphocytes:
 - B lymphocytes make antibodies which attack infecting bacteria, viruses, etc.
 - T lymphocytes help the B lymphocytes to make antibodies.
 - Natural killer cells which also help to protect against infection.
- All the other different blood cells (red blood cells, platelets, neutrophils, basophils, eosinophils and monocytes) develop from myeloid stem cells.

Blood production

You make millions of blood cells every day. Each type of cell has an expected life-span. For example, red blood cells normally last about 120 days. Some white blood cells last just hours or days - some last longer. Every day millions of blood cells die and are broken down at the end of their life-span. There is normally a fine balance between the number of blood cells that you make, and the number that die and are broken down. Various factors help to maintain this balance. For example, certain hormones in the bloodstream and chemicals in the bone marrow called 'growth factors' help to regulate the number of blood cells that are made.

The main types of leukaemia are:

- acute lymphoblastic leukaemia - 'ALL' (sometimes called acute lymphocytic leukemia).
- chronic lymphocytic leukaemia - 'CLL'.
- acute myeloid leukaemia - 'AML'.
- chronic myeloid leukaemia - 'CML'.

There are various 'subtypes' of each of these. In addition there are some other rare types of leukaemia. The word:

- 'acute' means the disease develops and progresses quite quickly.
- 'chronic' means persistent or ongoing. When talking about leukaemia the word chronic also means that the disease develops and progresses slowly (even without treatment).
- 'lymphoblastic' and 'lymphocytic' mean that an abnormal cancerous cell is a cell that originated from a lymphoid stem cell.
- 'myeloid' means that an abnormal cancerous cell is a cell that originated from a myeloid stem cell.

The rest of this leaflet is only about acute lymphoblastic leukaemia.

What is acute lymphoblastic leukaemia?

Acute lymphoblastic leukaemia (ALL) is a condition where the bone marrow makes large numbers of abnormal immature lymphocytes. The immature cells are called lymphoblasts. There are various sub-types of ALL. For example, the abnormal lymphoblasts can be immature B or T lymphocytes. The abnormal lymphoblasts continue to divide and multiply, but do not mature into proper lymphocytes. Typically, ALL develops quite quickly (acutely) and rapidly becomes worse (over a few weeks or so) unless treated.

Who gets acute lymphoblastic leukaemia?

ALL can occur at any age, but about 6 in 10 cases occur in children. It is the most common form of leukaemia to affect children (although it is an uncommon disease). It occurs in about 4 in 100,000 children each year. (There are between 400 and 500 new cases each year in the UK.) It can occur at any age in childhood, but most commonly develops between the ages of one and four years. Boys are more commonly affected than girls.

What causes acute lymphoblastic leukaemia?

A leukaemia is thought to first start from one abnormal cell. What seems to happen is that certain vital genes which control how cells divide, multiply, and die are damaged or altered. This makes the cell abnormal. If the abnormal cell survives it may multiply 'out of control' and develop into a leukaemia.

In most cases of ALL, the reason why an immature lymphocyte becomes abnormal and multiplies out of control is not known. There are certain 'risk factors' which increase the chance that leukaemia will develop, but these only account for a small number of cases. Risk factors include:

- Radiation. For example, previous radiotherapy for another condition.
- Past treatment with chemotherapy or other drugs that weaken the immune system.
- Certain genetic disorders, the most common being Down's syndrome.

One theory is that exposure to strong electromagnetic fields may be a risk factor. For example, living near power lines. However, recent research studies have found no evidence to support this theory as a cause of ALL.

What are the main symptoms and problems when ALL develops?

As large numbers of abnormal lymphoblasts are made, much of the bone marrow fills with these abnormal cells. Because of this, it is difficult for normal cells in the bone marrow to survive and make enough normal mature blood cells. Also, the abnormal lymphoblasts spill out into the bloodstream. Therefore, the main problems which can develop include:

- Anaemia. This occurs as the number of red blood cells goes down. This can cause tiredness, breathlessness and other symptoms. You also look pale.
- Blood clotting problems. This is due to low levels of platelets. This can cause easy bruising, bleeding from the gums, and other bleeding-related problems.
- Serious infections. The abnormal lymphoblasts do not protect against infection. Also, there is a reduced number of normal white blood cells which usually combat infection. Therefore, serious infections are more likely to develop. Depending on the type and site of infection which develops, the symptoms can vary greatly.

The abnormal lymphoblasts may also build-up in lymph glands and the spleen. You may therefore develop swollen glands in various parts of the body, particularly in the neck and armpits, and develop an enlarged spleen. Other common symptoms include an enlarged liver, pain in the bones or joints, persistent fever, and weight loss. Without treatment, ALL usually causes death within a few months.

How is acute lymphoblastic leukaemia diagnosed and assessed?

A blood test

A blood test can often suggest the diagnosis of ALL. The test will typically show a low number of red blood cells, normal white blood cells, and platelets. The blood test also typically shows a number of abnormal lymphoblasts which are not normally seen in the blood. So, the total 'white cell count' in the blood sample may be high, even though the number of normal white cells is low. Further tests are usually done to confirm the diagnosis.

A bone marrow sample

For this test a small amount of bone marrow is removed by inserting a needle into the pelvis bone (or sometimes the breastbone (sternum)). Local anaesthetic is used to numb the area. A small sample of bone may also be taken. The samples are put under the microscope to look for abnormal cells, and tested in other ways. This can confirm the diagnosis. (A separate leaflet describes bone marrow biopsy in more detail.)

Cell and chromosome analysis

Detailed tests are done on abnormal cells obtained from the bone marrow sample or blood test. These find out the exact type of cell that is abnormal. For example, if the abnormal cells are immature B lymphocytes or immature T lymphocytes. The chromosomes within the cells are checked for certain changes. Chromosomes are the parts in the cell which contain DNA - the genetic make-up of the cell. In some cases of ALL, changes can be detected to parts of one or more chromosome. (These chromosome changes only occur in the leukaemia cells, not the normal body cells.) For example, in one abnormality called Philadelphia chromosome, a part of chromosome 9 is found to be moved and attached to part of chromosome 22.

Lumbar puncture

This test collects a small amount of fluid from around the spinal cord (cerebrospinal fluid - CSF). It is done by inserting a needle between the vertebra in the lower (lumbar) region of the back. A separate leaflet describes this test in more detail. By examining the fluid for leukaemia cells, it helps to find out if the leukaemia has spread to the brain and spinal cord.

Various other tests

A chest x-ray, blood tests, and other tests are done to assess your general wellbeing.

What is the treatment for acute lymphoblastic leukaemia?

The aim of treatment is to kill all the abnormal cells. This then allows the bone marrow to function normally again, and produce normal blood cells. The main treatment is chemotherapy, sometimes combined with radiotherapy. Stem cell transplant is sometimes used.

The exact treatment regime used in each case (the drugs used, doses, length of treatment, etc) takes into account various factors. This is based on research trials which aim to determine the best treatment for the various sub-types of ALL. Research trials continue to try to find even better treatments. The factors which are taken into account include:

- The exact type of ALL (for example, if it is a T-cell or B-cell type).
- If the leukaemia cells contain chromosome changes such as the Philadelphia chromosome.
- Your age, sex and general health.
- The number of lymphoblasts in the blood at diagnosis.
- How well the condition responds to the initial phase of treatment (see below).
- Whether the leukaemia has spread to the brain and/or spinal cord.

On the basis of these factors, people with ALL are classed as 'low', 'standard' or 'high' risk. That is, the risk of the leukaemia coming back (relapsing) after 'standard' treatment. The type and intensity of treatment given can depend on your risk classification. For example, more intensive treatment is usually offered if your risk is 'high'.

Chemotherapy

Chemotherapy is a treatment which uses anti-cancer drugs to kill cancer cells, or to stop them from multiplying. (There is a separate leaflet which gives more details about chemotherapy.) As many doses of drugs are likely to be given straight into a vein (intravenous) over a prolonged period, it is usual for a plastic tube to be put into a large blood vessel and left for the duration of treatment. (This is a 'central line' or a 'PICC line'.) This enables drugs to be injected or 'dripped' into the large vein via the plastic tube without the need for repeated needle pricks.

Chemotherapy for ALL is usually divided into different 'phases'.

- Induction remission phase. This is an initial intensive treatment using a combination of drugs. It lasts about 4-6 weeks. This aims to kill most of the leukaemia cells. At the end of this phase there is usually no leukaemia cells detectable in a blood sample, or seen in a bone marrow sample. This is called being 'in remission'. Remission does not mean 'cure'. It means that no abnormal cells can be detected by tests.
- Consolidation (Intensification) phase. Further drugs are given in this phase of treatment. This aims to kill any remaining leukaemia cells which may still be present (although not detected by any tests). The treatment can be quite intensive, and given in 'blocks' of treatment several weeks apart. The exact drugs used and the intensity can vary, depending on factors such as whether you are in a high, standard or low risk category.
- Maintenance phase. This phase of treatment is less intensive than the induction and consolidation phases. It involves taking chemotherapy tablets each day, and an injection of a chemotherapy drug every few weeks. This phase can last up to two years or more. The aim of this phase is to kill any remaining leukaemia cells that may have been missed by the other phases. Maintenance treatment is also given between the blocks of treatment in the consolidation phase.

Treatment of the brain and spinal cord

Abnormal cells sometimes get into the brain and spinal cord. Chemotherapy drugs taken by mouth or injected into the bloodstream do not get into the brain and spinal cord very well. Therefore, chemotherapy drugs are usually injected from time to time over the treatment period directly into the fluid that surrounds the spinal cord and brain. This is done in a similar way to a lumbar puncture (described above) and is called an intrathecal injection. In some cases, radiotherapy to the brain is also used.

Stem cell transplantation

A stem cell transplant (SCT) (sometimes called bone marrow transplant) is not commonly used. It may be used for cases where the leukaemia has recurred following the usual treatment with chemotherapy. (See separate leaflet called '*Stem Cell Transplant*' for details.)

Supportive treatment

Other treatments include: antibiotics or antifungal drugs if infection occurs; blood transfusions to counter low levels of red blood cells and platelets; general supportive measures to overcome side-effects of chemotherapy.

Treatment of relapses

Despite treatment, in up to 1 in 4 cases, the ALL may return (relapse) at some point after treatment. Relapses are treated in a similar way to the initial treatment, but the treatment regime is often more intensive.

Side effects from chemotherapy

Your doctor will advise on the possible risks and side-effects of your particular treatment regime. Very briefly:

Side effects during treatment

The drugs used for chemotherapy are powerful and often cause unwanted side-effects. The drugs work by killing cells which are dividing and so some normal cells are damaged too. Side-effects

vary from drug to drug. The most common side effects are nausea (feeling sick), loss of hair, and an increased risk of infection (as the normal white blood cells are affected by treatment). Anti-sickness drugs are commonly used to prevent nausea.

Late side-effects

In a small number of cases, problems develop months or years after a period of intensive chemotherapy. For example, some children treated with chemotherapy have problems later in life with puberty and with fertility. There is also a small increased risk of developing a different cancer later in life.

What is the outlook (prognosis)?

Overall, the outlook is good. Most children with ALL (about 7-8 in 10 cases) can be cured and many adults with ALL are also cured. Your specialist will be able to give a more accurate prognosis. The chance of a good response to treatment can vary depending on factors such as the exact type of ALL.

Further help and information

CancerBACUP

3 Bath Place, Rivington Street, London, EC2A 3JR

Tel: 0808 800 1234 Web: www.cancerbacup.org.uk

Provides information and support to anyone affected by cancer or leukaemia.

Leukaemia Research Fund

Web: www.lrf.org.uk

Primarily involved in research and raises funds to these ends. Their web-site includes a comprehensive range of information for patients about leukaemia

Leukaemia Care

2 Shrubbery Avenue Worcester WR1 1QH

Careline: 0800 169 6680 Web: www.leukaemiacare.org.uk

Aims to promote the welfare of those suffering from Leukaemia and allied blood disorders.

Cancer Research UK

Their website www.cancerhelp.org.uk provides facts about cancer and leukaemia including treatment choices.

Other support groups

See [Cancer Support Groups](#) at www.patient.co.uk for a list of self help and support groups for cancer and leukaemia patients.

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