

Acute Lymphoblastic Leukaemia (A L L)

J A S C A P

JEET ASSOCIATION FOR SUPPORT TO CANCER PATIENTS, MUMBAI, INDIA

JASCAP
JEET ASSOCIATION FOR SUPPORT TO CANCER PATIENTS

c/o. Abhay Bhagat & Co., Office No.4, "Shilpa", 7th.Road, Prabhat Colony,
Santacruz (East), Mumbai – 400 055

Tel.: 2617 7543, 2616 0007. Fax: 91-22-2618 6162
E-mail :pkrajscap@gmail.com & abhay@abhaybhagat.com

JASCAP is a charitable trust that provides information on various aspects of cancer. This can help the patient and his family to understand the disease and its treatment and thus cope with it better.

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Contact: Mr. Prabhakar K. Rao or Mrs. Neera P. Rao

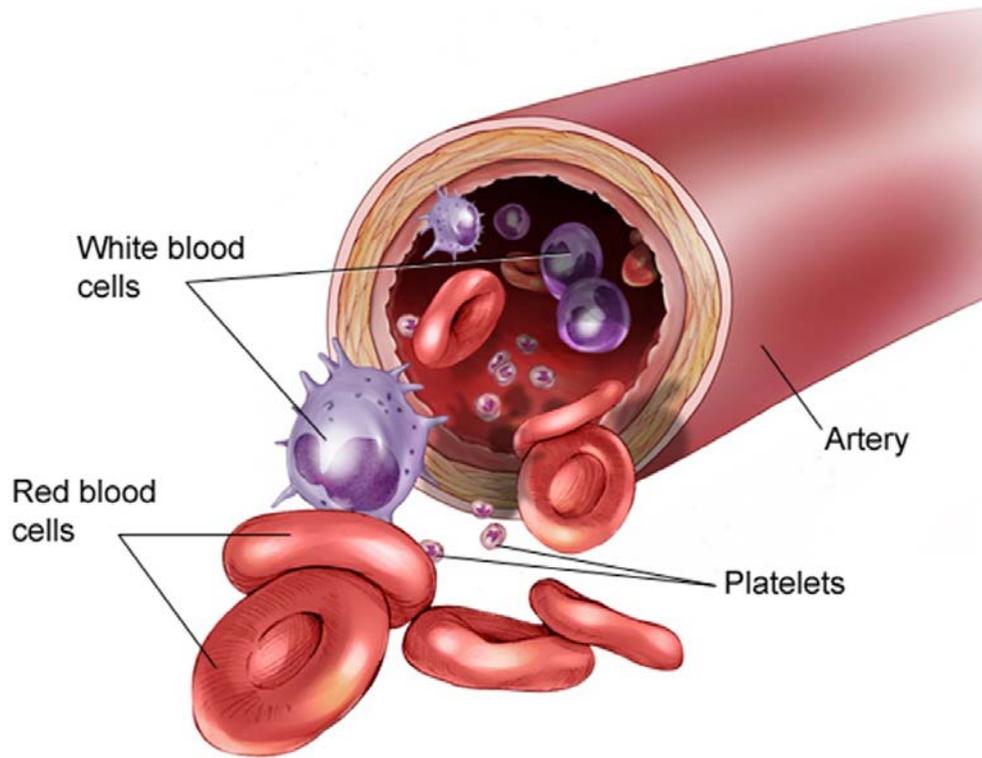
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Anatomy of Red Blood Cells, White Blood Cells and Platelets

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Acute Lymphoblastic Leukaemia (ALL)

Introduction

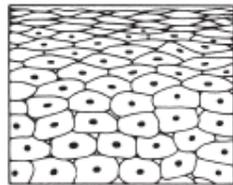
This booklet is for you if you have or someone close to you has Acute Lymphoblastic Leukaemia.

If you are a patient your doctor or nurse may wish to go through the booklet with you and mark sections that are particularly important for you.

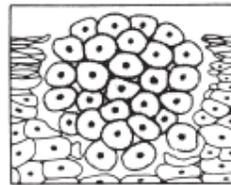
What is cancer?

The organs and tissues of the body are made up of tiny building blocks called cells. Cancer is a disease of these cells.

Cells in different parts of the body may look and work differently but most reproduce themselves in the same way. Cells are constantly becoming old and dying, and new cells are produced to replace them. Normally, cells divide in an orderly and controlled manner. If for some reason the process gets out of control, the cells carry on dividing, developing into a lump which is called a **tumour**.



Normal cells



Cells forming a tumour

Not all tumors are cancerous. Tumors that aren't cancer are called **benign**. Benign tumors can cause problems -- they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize – see below). These tumors are almost never life threatening.

Cancer is the name given to a **malignant** tumour. Doctors can tell if a tumour is benign or malignant by examining a small sample of cells under a microscope. This is called a **biopsy**.

A malignant tumour consists of cancer cells that have the ability to spread beyond the original area. If the tumour is left untreated, it may spread into and destroy surrounding tissue. Sometimes cells break away from the original (primary) cancer. They may spread to other organs in the body through the bloodstream or lymphatic system.

The lymphatic system is part of the immune system - the body's natural defence against infections and diseases. It is a complex system made up of organs, such as

bone marrow, the thymus, the spleen, and lymph nodes. The lymph nodes (or glands) throughout the body are connected by a network of tiny lymphatic ducts.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called **secondary cancer** or **metastasis**. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

It is important to realise that cancer is not a single disease with a single type of treatment. There are more than 200 different kinds of cancer, each with its own name and treatment.

Types of cancers

Carcinomas

The majority of cancers, about 85% (85 in a 100), are carcinomas. They start in the epithelium, which is the covering (or lining) of organs and of the body (the skin). The common forms of breast, lung, prostate and bowel cancer are all carcinomas.

Carcinomas are named after the type of epithelial cell that they started in and the part of the body that is affected. There are four different types of epithelial cells:

- squamous cells - that line different parts of the body, such as the mouth, gullet (oesophagus), and the airways
- adeno cells - form the lining of all the glands in the body and can be found in organs such as the stomach, ovaries, kidneys and prostate
- transitional cells - are only found in the lining of the bladder and parts of the urinary system
- basal cells - that are found in one of the layers of the skin.

A cancer that starts in squamous cells is called a squamous cell carcinoma. A cancer that starts in glandular cells is called an adenocarcinoma. Cancers that start in transitional cells are transitional cell carcinomas, and those that start in basal cells are basal cell carcinomas.

Leukaemias and lymphomas

These occur in the tissues where white blood cells (which fight infection in the body) are formed, i.e. the bone marrow and lymphatic system. Leukaemia and lymphoma are quite rare and make up about 6.5% (6.5 in 100) of all cancers.

Sarcomas

Sarcomas are very rare. They are a group of cancers that form in the connective or supportive tissues of the body such as muscle, bone and fatty tissue. They account for less than 1% (1 in 100) of cancers.

Sarcomas are split into two main types:

- bone sarcomas - that are found in the bones
- soft tissue sarcomas - that develop in the other supportive tissues of the body.

Others forms of cancer

Brain tumours and other very rare forms of cancer make up the remainder of cancers.

Blood – Structure and Function

Blood is made up of blood cells suspended in liquid called plasma. There are three main types of blood cells:

- red cells, which carry oxygen around the body
- platelets, which help the blood to clot and control bleeding
- white cells, which fight infection.

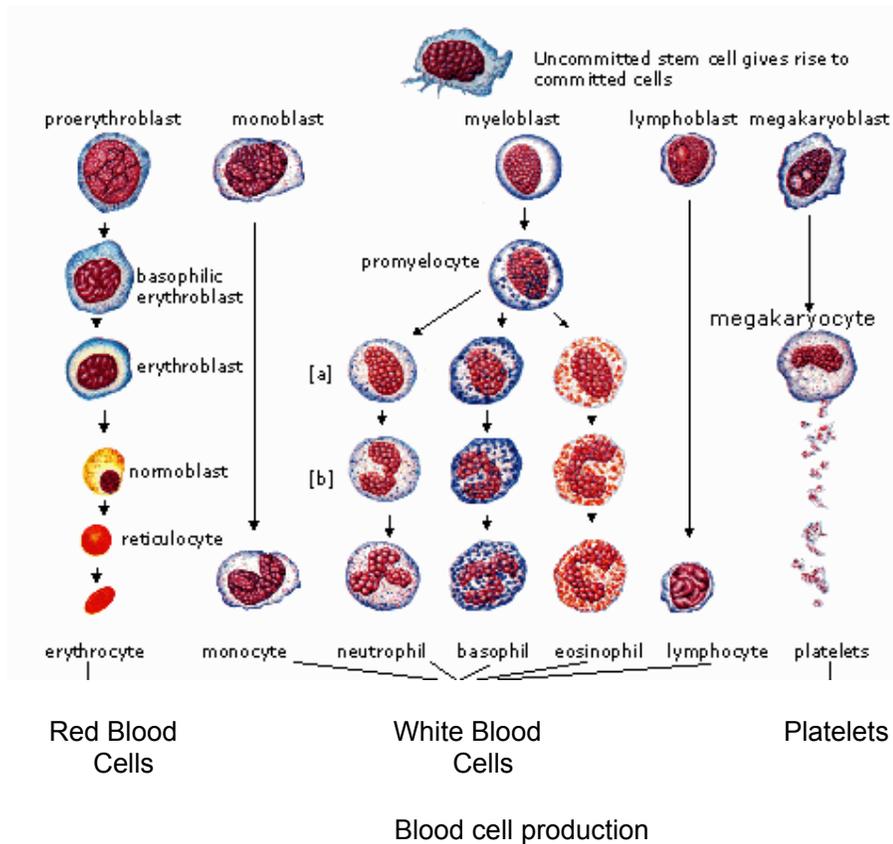
How blood cells are made?

Blood cells are made in the bone marrow, a spongy material inside the bones. Normally millions of new blood cells are made every day to replace old and worn out blood cells.

All blood cells begin as a special type of cell called a stem cell. There are two types:

- **Lymphoid stem cells** make white blood cells called lymphocytes.
- **Myeloid stem cells** make all the other types of blood cells: red cells, platelets and white cells called granulocytes.

Stem cells make new blood cells by copying themselves and then dividing to form two new cells. To begin with the new blood cells made from stem cells are immature. They don't look like red cells, white cells or platelets and they can't do the jobs in the body that they can do. These immature cells are called blast cells. Normally blast cells stay in the bone marrow until they have matured into red cells, white cells or platelets.



The bone marrow

Blood is made in the bone marrow. This is a spongy material that's found in the middle of your bones, particularly in your pelvis and backbone (spine).

All your blood cells are made from special cells called **stem cells**. The bone marrow gives the stem cells a safe place to divide and grow to form fully developed (mature) red cells, platelets and white cells.

These are then released into your blood to carry out different functions:

- Red blood cells contain **haemoglobin**, which carries oxygen from your lungs to all the cells in your body.
- White blood cells fight and prevent infection. There are several types of white cell. The two most important types are **neutrophils** and **lymphocytes**.
- Platelets are very small cells that help the blood to clot and prevent bleeding and bruising.

The levels of these cells in your blood are measured in a blood test called a **full blood count (FBC)**. The figures below are a guide to the levels usually found in a healthy person.

Type of blood cell or element	Levels found in a healthy person
Haemoglobin (Hb)	13–18g/dl (men) 11.5–16.5g/dl (women)
Platelets	150–400 x 10 ⁹ /l
White cells (WBC)	4.0–11.0 x 10 ⁹ /l
Neutrophils	2.0–7.5 x 10 ⁹ /l
Lymphocytes	1.5–4.5 x 10 ⁹ /l

These figures can vary from hospital to hospital. Your doctor or nurse will be able to tell you what levels they use. They can also be slightly different in people of African-Caribbean and Middle Eastern origin.

The figures might look complicated when they're written down, but in practice they are used in a straightforward way. For example, you'll hear doctors or nurses saying things like 'your haemoglobin is 14' or 'your neutrophils are 4'. Many people with CML soon get used to these figures and what they mean.

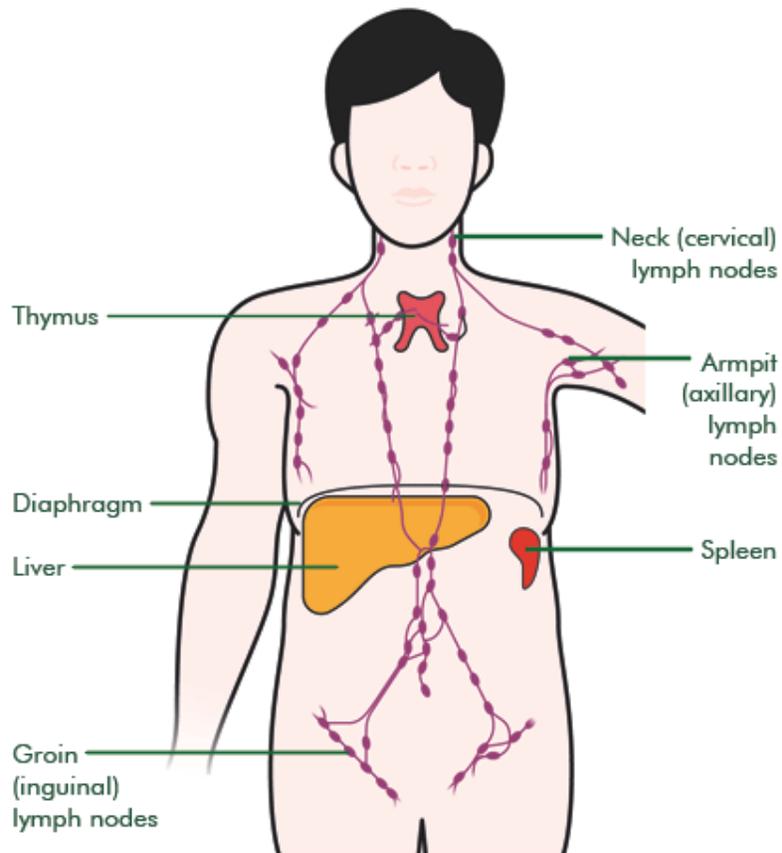


Figure: The lymphatic system

White blood cells

There are two main types of white blood cell: lymphocytes and myeloid cells (also known as granulocytes). These cells work together to fight infection. Some myeloid cells and lymphocytes only live for a few days, so the bone marrow is constantly making new cells to replace the old ones in the blood.

The bone marrow normally makes millions of blood cells every day. When they're mature enough to leave the bone marrow, the white blood cells are released into the bloodstream to circulate around the body. Lymphocytes, unlike the myeloid cells, also circulate in the lymphatic system.

The lymphatic system is one of the body's natural defences against infection. It's a complex system made up of lymphatic organs such as bone marrow, tonsils, the spleen and a collection of small lymph nodes (sometimes called glands).

The lymph nodes produce lymph, a milky-looking fluid containing lymphocytes. The lymph nodes are found mainly in the neck, armpit and groin and are connected by a network of tiny lymphatic vessels.

The tonsils, liver, spleen (which breaks down old blood cells) and bone marrow also contain lymphocytes. There are two main types of lymphocyte: B-cells and T-cells.

What is Leukaemia?

Leukaemia is a cancer of the bone marrow. It affects the cells in the bone marrow that produce white blood cells.

The four main types of leukaemia are:

- acute lymphoblastic (ALL)
- acute myeloid (AML)
- chronic lymphocytic (CLL)
- chronic myeloid (CML).

Each type has its own characteristics and treatment.

What is Acute Lymphoblastic Leukaemia (ALL)?

Acute lymphoblastic leukaemia (ALL) is a rare type of cancer, affecting approximately 200 adults per year in the UK.

ALL is a cancer of the white blood cells. Normally, white blood cells grow and divide in an orderly and controlled way. In leukaemia this process gets out of control as the normal signals that stop the body making too many cells are ignored. So the cells go on dividing and do not mature.

In ALL there is an overproduction of immature lymphocytes, called lymphoblasts (sometimes referred to as blast cells).

These immature cells fill up the bone marrow and stop it from making blood cells properly. As the lymphoblasts do not mature, they can't do the work of normal white blood cells (fight infection). Also, because the bone marrow is overcrowded with immature white cells, it can't make enough healthy red cells and platelets.

ALL occurs most frequently in children under 15; in adults it is more common between the ages of 15–25 and in older people. It's slightly more common in males than in females.

Risk factors and causes of ALL

The cause of ALL is not known, but research is going on all the time to find out. Like other cancers, ALL is not infectious and can't be passed on to other people.

Research has shown that a person's risk of developing ALL is NOT significantly increased by:

- exposure to electromagnetic fields
- living near high-voltage electricity cables
- household radon.

However, there are a number of risk factors that may increase a person's risk of developing it. These are:

Radiation

Exposure to very high radiation levels (such as during a nuclear accident or an atom bomb) is known to increase the risk of developing ALL. However, very few people in the UK will be exposed to radiation levels high enough to increase their risk.

In recent years there has been publicity about the increase in leukaemia in people living close to nuclear power plants. Research is still underway to see if there is any definite link, but currently there is no evidence of this.

Genetic conditions

ALL is not caused by an inherited faulty gene, so members of your family do not have an increased risk of developing it just because you have it. People with certain genetic disorders, including Down's syndrome and Fanconi's anaemia, are known to have a higher risk of developing leukaemia.

Exposure to chemicals

In very rare cases, leukaemia may occur in people who have been exposed to chemicals used in industry, such as benzene and other solvents.

Infection

It is thought that ALL occurs due to a series of genetic changes in a particular group of immature blood cells. What causes the genetic changes is not fully understood, but infection may be involved in the process. However, no specific infections that cause leukaemia have been found.

How common is Lymphoblastic leukemia in India?

Leukemia is one of the common types of cancer in India. The incidence (newly diagnosed cases of Cancer in a year) of all types of leukemias together (Acute and Chronic; Lymphoblastic, Pro-myelocytic and Myeloid) is about 4 persons per 1,00,000 population¹.

In India, between the years 2001-2003, across five urban centers - Mumbai, Delhi, Chennai, Bhopal and Bangalore, – and one rural center - Barshi, a total of 1,039 cases of Lymphoblastic leukemia (both Acute and Chronic combined) were registered (2.36% of all cancers) for males across all age groups; while 521 cases of Lymphoblastic leukemia (both Acute and Chronic combined) were registered (1.17% of all cancers) for females across all age groups. Considering all men, women and children with all types of cancers together, a grand total of 1,560 cases of Lymphoblastic leukemia (both Acute and Chronic combined) (1.76% of all cancers) were registered at the six centers mentioned above, between the year 2001-2003².

The TATA Memorial Hospital (T.M.H.) in Mumbai, India registered a grand-total of 19,127 cases of all types of cancer patients in the year 2006, for men, women and children combined, out of which 456 (2.4% of the total cases) were diagnosed with the Lymphoblastic leukemia (both Acute and Chronic combined). Out of the total 456 patients diagnosed with Lymphoblastic leukemia (both Acute and Chronic combined), mentioned above at the T.M.H., 333 (73%) were males and 123 (27%) were females³.

Eighteen percent of all Haematopoietic cancers among men, women and children in the year 2006 at the T.M.H. were attributable to Lymphoblastic leukemia (both Acute and Chronic combined).

Symptoms and Diagnosis

How ALL is diagnosed?

Usually you will see your GP, who will examine you and take a blood test. If the results of the test are abnormal in any way, your GP or a haematologist from the local hospital will contact you. A haematologist is a doctor who specialises in the treatment of blood problems. They will arrange for you to be seen quickly at the hospital for further tests and treatment.

¹ Globocan 2008: Cancer incidence and mortality rates worldwide

² Population based cancer registry 2001-2003 Mumbai, Delhi, Chennai, Bhopal, Barshi and Bangalore, Indian Cancer Society.

³ TATA Memorial Hospital Registry Data for 2006

Further tests for ALL

Most people with ALL are referred for treatment at a specialist haematology unit in the hospital. The doctor at the hospital will take your full medical history before doing a physical examination and a blood test to check the numbers of all the different types of blood cell.

If the blood test shows that leukaemia cells are present, your doctor will want to take a sample of your bone marrow. This is the most important test to find out the exact type of leukaemia you have, and gives information that the doctors need to plan the best treatment for you.

Bone marrow sample/biopsy.

A small sample of bone marrow is taken from the back of the hip bone (pelvis) or occasionally the breast bone (sternum). It is looked at under a microscope to see if it contains any abnormal white blood cells. A haematologist can tell which type of leukaemia it is by identifying the type of abnormal white cell. Other tests will be carried out on the bone marrow sample to help confirm the diagnosis. Before the bone marrow sample is taken you are given a local anaesthetic injection to numb the area. A needle is then passed through the skin into the bone. A small sample of the bone marrow is drawn into a syringe to be examined under a microscope.

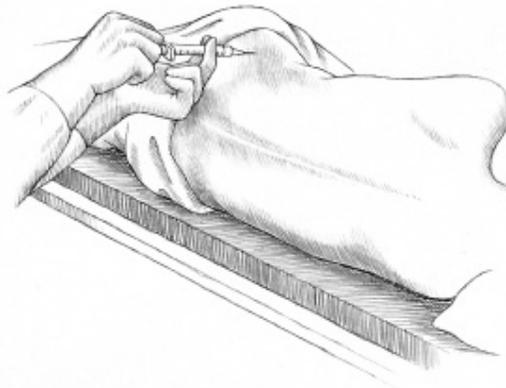


Figure: A bone marrow sample being taken

The procedure can be done on the ward or in the outpatients department, and takes about 15–20 minutes.

It may be uncomfortable when the marrow is drawn into the syringe, but this should only last a short time. You may be offered a short-acting sedative to reduce any pain or discomfort during the test.

Sometimes a small core of marrow is needed (a trephine biopsy) and this procedure takes a few minutes longer. A special type of needle is passed through the skin into the bone marrow. This can cut out a sample of the bone marrow.

You may feel bruised after the test and have an ache for a few days. This can be eased with mild painkillers.

Cytogenetics

Each cell in the body contains chromosomes, which are made up of genes. The genes control all activities of the cell. In leukaemia there are often changes in the structure of the chromosomes within the leukaemic cells, but not the normal cells of the body.

The tests on the blood and bone marrow sample will include a chromosome analysis to look for any particular changes in the chromosomes. Different types of leukaemia are associated with particular genetic changes. These tests, known as cytogenetic tests, can help to decide the best treatment and predict how well the leukaemia may respond to that treatment.

Immunophenotyping

Another test on the blood or bone marrow sample will show which type of lymphocyte has become cancerous. Immunophenotyping can tell the doctors whether your leukaemia developed from B-lymphocytes or T-lymphocytes. Knowing which type of lymphocyte is affected helps the doctors plan the most appropriate treatment.

Chest x-ray

This is taken to check for any sign of swollen lymph glands in the chest.

Lumbar puncture

A small sample of the fluid that surrounds your brain and spinal cord is taken to check for leukaemia cells. Your doctor uses a local anaesthetic to numb the lower part of your back and passes a needle gently into the spine to draw off a tiny sample of the fluid.

Having the lumbar puncture may be uncomfortable, but it only takes a few minutes. Some people may have a headache afterwards. If this happens let your doctor know so that they can prescribe painkillers for you. You may need to lie flat for a few hours afterwards.

Scans

Scans – such as a CT, MRI and ultrasound scan – may be done to find out if the leukaemia has spread to other parts of your body. Your doctor or specialist nurse can tell you about any scans that may be necessary.

It will probably take several days for the results of your tests to be ready, and this waiting period will obviously be an anxious time for you. It may help if you can find a close friend or relative to talk things over with. You can also contact our cancer support specialists.

Symptoms of ALL

The main symptoms of ALL are caused by the increased number of immature cells (blast cells) in the blood, which reduces the number of normal blood cells.

Symptoms of ALL include:

- Looking pale – which may be due to anaemia caused by a lack of red blood cells.
- Feeling very tired – even breathless, at the slightest effort.
- Feeling generally unwell and run-down – perhaps with a sore throat or sore mouth.
- Aching joints and bones – the bones can be affected by leukaemia cells.
- Having various infections one after the other – caused by a lack of healthy white blood cells.
- Unusual bleeding – caused by a reduction in the number of platelets. This may include bruising (bruises may appear without any apparent injury), heavy periods in women, bleeding gums and frequent nosebleeds.

Occasionally, a person will not have any of these symptoms and the leukaemia is discovered during a routine blood test.

Symptoms may appear very quickly over a few weeks, and treatment needs to be given as soon as possible. If you have any of these symptoms you should have them checked by your doctor, but remember they are common to many illnesses other than leukaemia.

Classification of ALL

There are different sub-types of ALL based on the type of lymphocyte (either B- or T-lymphocyte) that has become cancerous.

The World Health Organisation (WHO)'s classification system is used for planning treatment and predicting response. There are three different sub-types:

- early (precursor) B-lymphoblastic leukaemia (most adults with ALL have this type)
- mature B-lymphoblastic leukaemia (sometimes called Burkitt-type ALL because it is similar to Burkitt's lymphoma)
- early (precursor) T-lymphoblastic leukaemia.

Philadelphia chromosome

Some people with ALL have a particular genetic abnormality known as a Philadelphia chromosome. The Philadelphia chromosome develops when part of chromosome 9 (the ABL gene) wrongly attaches to chromosome 22 (the BCR gene) during cell division.

This creates a new gene, known as BCR-ABL, which produces a specific new protein. The protein causes the production of an enzyme called tyrosine kinase, which makes the bone marrow produce abnormal blood cells.

The Philadelphia chromosome isn't inherited and can't be passed on to your children.

Treatment for ALL

Treatment Overview

The aim of treatment for ALL is to destroy the leukaemia cells and allow the bone marrow to work normally again.

When there is no sign of the leukaemia and the marrow is working normally this is called remission. With treatment, 8 out of 10 adults with ALL (80%) will go into remission. For some, this lasts indefinitely and the person is said to be cured.

Multidisciplinary team approach

Your treatment will be planned by a team of doctors and other staff at your hospital, known as a multidisciplinary team. The team normally includes:

- one or more haematologists who diagnose the leukaemia in collaboration with specialist laboratory scientists
- a clinical oncologist (a doctor who specialises in radiotherapy and chemotherapy)
- specialist nurses who give information and support.

Other staff are available to help if necessary, such as social workers, dietitians, counsellors and psychologists and physiotherapists.

When they are planning your treatment, they will consider a number of factors, including:

- the type of ALL you have
- any chromosomal abnormalities within the leukaemia cells
- your age and general health.

In the UK, treatment for ALL is given according to guidelines which have been agreed by specialists and are based on the results of trials and research. You may be asked to take part in a trial of a new and possibly better treatment.

Chemotherapy (drug treatment) is the main type of treatment given for ALL. The chemotherapy is carried in the bloodstream to nearly all parts of the body, but does not reach the brain and spinal cord.

The brain and spinal cord are known as the central nervous system (CNS). Additional treatment is needed to prevent the leukaemia affecting the CNS; this is known as CNS directed therapy. It involves giving chemotherapy into the fluid around the brain and spinal cord, which may be combined with radiotherapy to the brain. In men, the chemotherapy does not reach the testes, so they may also be given radiotherapy to the testes.

Giving your consent

Before you have any treatment, your doctor will explain its aims. They will usually ask you to sign a form saying that you give your permission (consent) for the hospital

staff to give you the treatment. No medical treatment can be given without your consent, and before you are asked to sign the form you should have been given full information about:

- the type and extent of the treatment you are advised to have
- the advantages and disadvantages of the treatment
- any other possible treatments that may be available
- any significant risks or side effects of the treatment.

If you don't understand what you have been told, let the staff know straight away so that they can explain again. Treatments for leukaemia can be complex, so it is common for people to need further explanations.

It is often a good idea to have a friend or relative with you when the treatment is explained, to help you remember the discussion more fully.

You may also find it useful to write down a list of questions before you go to your appointment.

Patients may feel that the hospital staff are too busy to answer their questions, but it's important for you to be aware of how the treatment is likely to affect you. The staff should be willing to make time for you to ask questions.

You can always ask for more time to decide about the treatment if you feel that you can't make a decision when it's first explained to you.

You are also free to choose not to have the treatment. It's important that you understand what will happen if you don't have treatment. The medical staff will need to record your decision in your medical notes. They can also explain what support may be available if this is your choice.

The benefits and disadvantages of treatment

Many people are frightened by the idea of cancer treatment because of the side effects that can occur. Some people ask what will happen if they do not have treatment.

Although many of the treatments can cause side effects, these can often be controlled or reduced with medicines. Treatment can be given for different reasons and the aims and possible benefits will vary depending upon the individual situation.

If the aim of your treatment is to achieve a remission and cure for your leukaemia, deciding whether to have the treatment may not be difficult.

However, if the treatment is being given just to control the leukaemia for a time, it may be more difficult to decide whether to go ahead. Making decisions about treatment in these circumstances is always difficult, and you may need to discuss this issue in detail with your doctor. If you choose not to have treatment, you can still be given supportive (palliative) care, with medicines to control any symptoms.

If you want to stop your treatment, it's important to tell a doctor or the nurse in charge. They can discuss your decision with you and offer you the best advice. They will also make a record of your decision in your medical notes.

Second opinion

Your multidisciplinary team will use national treatment guidelines to decide on the most suitable treatment for you. Even so, you may want to have another medical opinion. Your specialist or GP may be willing to refer you to another specialist for a second opinion, if you feel it will be helpful. However, getting a second opinion can take some time to arrange. Treatment for ALL usually needs to be started as soon as possible so there may not be enough time to arrange a second opinion.

If you do go for a second opinion, it may be a good idea to take a friend or relative with you, and have a list of questions ready so that you can make sure your concerns are covered during the discussion.

Chemotherapy for ALL

Chemotherapy uses anti-cancer (cytotoxic) drugs to destroy the leukaemia cells. These work by disrupting the production of the leukaemia cells.

Chemotherapy drugs circulate all over the body in the bloodstream. However, the chemotherapy drugs can't get into the fluid around the brain and spinal cord (cerebrospinal fluid – CSF), so they need to be injected directly into the fluid through a lumbar puncture. This is done even if leukaemia cells can't be detected in the CSF, as research has shown that there will almost always be some leukaemia cells in the CSF which need to be destroyed.

For people who have just been diagnosed with ALL it's important to start treatment quickly. Treatment is divided into three different phases:

Induction

This is the initial intensive phase of treatment, aimed at destroying as many leukaemia cells as possible. It usually achieves a remission of the disease. Common chemotherapy drugs which may be used in this phase include:

- vincristine
- daunorubicin or doxorubicin
- methotrexate
- crisantapase (asparaginase)
- mercaptopurine
- cyclophosphamide

Steroids are also given as part of the treatment. You may also have a drug called allopurinol which helps to protect the kidneys against damage caused by the increase in uric acid (a waste chemical produced when the leukaemia cells are destroyed).

Some people who have the Philadelphia chromosome may be given a drug called imatinib (Glivec®).

The induction phase of treatment normally lasts 3–8 weeks. As this is a very intense phase, you'll need to stay in hospital for about four weeks. This is because you're likely to need antibiotics and drips (infusions) of red blood cells and platelets.

Intensification (consolidation)

After the induction phase, more chemotherapy is given to increase the chance of destroying any remaining leukemia cells that cannot be seen in the blood or bone marrow. Drugs used during consolidation may include:

- Cytarabine
- Etoposide
- Thioguanine (thioguanine)

as well as some of the same drugs used during induction.

The consolidation phase of the treatment usually lasts for several months.

Continuing therapy (maintenance)

This treatment reduces the risk of the leukaemia coming back at a later stage after treatment has finished. It's a less intensive course of chemotherapy. Common drugs used are mercaptopurine and methotrexate, which are given as tablets, and vincristine, which is given by injection. Steroids are usually continued in short courses.

This phase may last for a couple of years and is usually given as an outpatient. You don't usually need to be admitted to hospital unless you develop problems such as an infection.

Throughout these three phases of your treatment you'll have regular blood tests and lumbar punctures to check for leukaemia cells. Your doctor will check the results of these and will make changes to your treatment if needed.

Instead of standard-dose maintenance chemotherapy, some people will have high-dose chemotherapy with a stem cell transplant. This may be given to increase the chances of a cure. It may also reduce the possibility of a relapse if someone has risk factors which make it more likely for the ALL to come back.

The high-dose treatment may include radiotherapy to the whole body (known as total body irradiation or TBI) and high doses of a chemotherapy drug such as etoposide or busulfan.

If you have standard continuing chemotherapy, your complete chemotherapy course is likely to last for at least two years. If you have high-dose chemotherapy after the induction and intensification phases, the treatment time may be shorter and may finish in less than a year.

How the chemotherapy is given

The main induction and intensification treatments consist of a combination of three or four drugs given by injection into a vein (intravenously), and some drugs which are given as tablets.

Central lines

To make having chemotherapy easier and to prevent you from having frequent injections, a plastic tube (called a central line) can be put into a vein in your chest. The tube is put in under a general or local anaesthetic. Usually a small cut (incision) is made in the skin over your chest, and a narrow flexible plastic tube is placed under your skin and into a large vein in your neck. The other end of the tube stays outside your body and has a screw cap at the end. The tube can be used to give drugs, fluids, stem cells or bone marrow, and also to collect blood samples.

You may feel sore and uncomfortable for a couple of days after the line has been put in, but it should then be painless. It can stay in for as long as it's needed, which may be more than two years. The nurses will show you how to look after it to prevent blockages or infections.

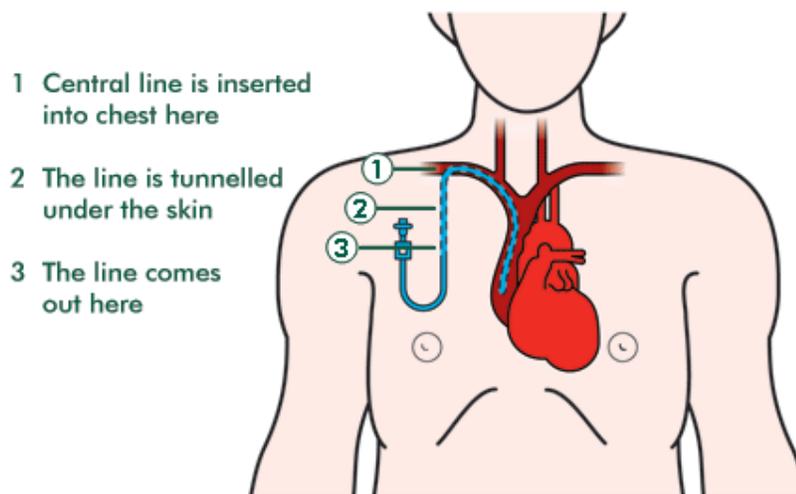


Figure: A central line

PICC lines and implantable ports

Instead of a central line, a PICC line (peripherally inserted central venous catheter) or an implantable port may be used. A PICC line is a long, thin tube put into a vein in the crook of the arm. An implantable port is a thin, soft plastic tube that is put into a vein in the chest and has an opening (port) just under the skin of the chest or arm.

Your doctor or chemotherapy nurse will explain the procedure to you. You will be given a local anaesthetic before the line is put in.

Intrathecal chemotherapy

As is done by injection into a vein, chemotherapy for ALL is often given directly into the fluid around the brain and spinal cord (cerebrospinal fluid). Giving chemotherapy in this way is known as intrathecal chemotherapy. This is done using a similar procedure to the lumbar puncture. After giving a local anaesthetic, the doctor gently puts a needle into the fluid in the spine, a small amount of fluid is drawn off and the drugs are injected. The drugs will help to destroy any leukaemia cells in the fluid.

Supportive care

During your treatment you will also need treatment for the symptoms that have been caused by a lack of normal blood cells due to the leukaemia itself and the chemotherapy.

Drips (transfusions) of red blood cells and platelets are usually needed to replace the normal blood cells. Antibiotics may also be needed to prevent and treat any infections. These can also be given through your central line.

Side effects of chemotherapy

Risk of bruising and bleeding

Platelets help blood to clot. With leukaemia, the number of platelets in your blood is lower than normal, and chemotherapy may temporarily reduce the numbers even more.

This means that you may develop blood spots or rashes on the skin (called petechiae), bruise very easily, have nosebleeds or bleed more heavily from even minor cuts and grazes.

You may need to have a drip (transfusion) of platelets before your chemotherapy begins, and at times during your treatment, to replace the missing platelets. We can send you a fact sheet about platelet transfusions.

If you develop any unexplained bruising or bleeding, such as nosebleeds, blood spots, rashes on the skin or bleeding gums contact the hospital immediately.

Low resistance to infection

While the chemotherapy drugs are acting on the leukaemia cells in your body, they also reduce the number of normal cells in your blood for a while. When the white cells are low (known as neutropenia), you are more likely to get an infection.

During chemotherapy your blood will be tested regularly. You'll probably be given tablets or other medicines to reduce the risk of infection.

If you get an infection, you'll be given medicines to treat it. Most infections are caused by bacteria or viruses already in your own body. These do not normally cause infection, but when your immunity is low they are more likely to cause a problem.

It's best to avoid coming into contact with someone who may have an infection. You may also be advised to be careful about what you eat, to guard against the risk of infection from raw, undercooked or contaminated food. The hospital will give you information on how to prepare foods and which foods to avoid.

If your temperature goes above 38°C (100.4°F) or you suddenly feel ill, even with a normal temperature, contact your doctor or the hospital straight away.

You may be given injections of a drug called G-CSF (granulocyte-colony stimulating factor). This is a type of protein that stimulates the bone marrow to produce more white blood cells. The injections are given under the skin (subcutaneously).

Anaemia

If the level of red blood cells (haemoglobin) in your blood is low you may become very tired and lethargic. You may also become breathless. These are all symptoms of anaemia – a lack of haemoglobin in the blood.

Anaemia can be treated very successfully by blood transfusions. You should quickly feel more energetic after a transfusion and the breathlessness will be eased. We can send you a fact sheet about blood transfusions.

Tiredness (fatigue)

This is a common effect of chemotherapy. The fatigue may be due to anaemia, but may also occur as a result of chemotherapy, even if your blood count is normal. You may be especially aware of this when you're at home between courses of chemotherapy and for a few months after the treatment.

Feeling sick

Some of the drugs used to treat ALL may make you feel sick (nausea) and may sometimes cause vomiting. There are very effective anti-sickness drugs (anti-emetics) to prevent or greatly reduce nausea and vomiting, which your doctor can prescribe for you. Let them know if the anti-emetics are not controlling your nausea as they can prescribe different ones.

Sore mouth

Some chemotherapy drugs can make your mouth sore and cause mouth ulcers. Regular mouthwashes are important and your nurse will show you how to use these properly.

If you don't feel like eating during treatment, you could try replacing some meals with nutritious drinks or a soft diet.

Effects on the heart

Some of the drugs used to treat ALL may affect the heart muscle. The doses of the chemotherapy drugs are very carefully monitored, and heart tests (such as cardiac echograms) may be done from time to time to check your heart.

Hair loss

Unfortunately, hair loss is another common side effect of these drugs. If your hair falls out, you can cover your head by wearing wigs, hats or scarves. Most patients are entitled to a free wig from the NHS. Your doctor or one of the nurses on the ward can usually arrange for a wig specialist to visit you.

If your hair falls out, it will grow back over a period of 3–6 months when the treatment ends.

Although they may be hard to deal with at the time, these side effects will disappear once your treatment is over.

Coping with chemotherapy

Chemotherapy affects different people in different ways. Many people find that there are times during their treatment when they feel very unwell and tired and have to take things much more slowly. Do as much as you feel like and rest whenever you need to.

Contraception

It is not advisable to become pregnant or father a child while taking any of the chemotherapy drugs used to treat ALL, as they may harm the developing baby. It's important to use effective contraception during your treatment and for a few months afterwards. You can discuss this with your doctor or nurse.

Condoms should be used during sex for the first 48 hours after chemotherapy in order to protect your partner from any of the drug that may be present in semen or vaginal fluid.

Radiotherapy for ALL

Radiotherapy treats cancer by using high-energy rays which destroy the cancer cells, while doing as little harm as possible to normal cells.

Radiotherapy may be given to the head as part of CNS directed therapy. In some men it may also be given to the testes.

The course of treatment is given in the hospital radiotherapy department, usually in 8–10 sessions from Monday–Friday over two weeks, with a rest at the weekend. Your doctor will discuss your treatment with you in detail beforehand.

If you need to have high-dose treatment with stem cell support you may have a special form of radiotherapy called total body irradiation, or TBI. Radiotherapy is given to the whole body to destroy the bone marrow cells.

Planning your Radiotherapy treatment

Planning is a very important part of radiotherapy and may take a few visits. Careful planning makes sure that the radiotherapy is as effective as possible. It ensures the radiotherapy rays are aimed precisely at the cancer and cause the least possible damage to the surrounding healthy tissues.

The treatment is planned by your clinical oncologist, a physicist and sometimes by a senior radiographer. You may have your first treatment on the same day as your planning session, but usually it's necessary to wait a number of days while the team (physicist, oncologist or radiographer) prepare the final details.

The first step is to make sure that you lie in exactly the same position for each treatment. On your first few visits to the radiotherapy department you'll lie under a large machine called a simulator, which takes x-rays of the area to be treated. Sometimes a CT scanner may be used for the same purpose.

For cranial radiotherapy you may be fitted with a special clear plastic mask which is moulded to the exact size of your head and neck. This can be attached to the treatment couch and makes sure that your head stays in the correct position. Marks are made on the mask to show the treatment area.

If you're not wearing a mask for treatment, marks will be drawn on your skin. This helps the radiographer, who operates the machine and gives you your treatment, to position you accurately and to show where the rays are to be aimed.

These marks must stay visible throughout your treatment but they can be washed off once your treatment is over. Sometimes, you may have tiny permanent marks (like tattoos) on your skin. These will only be made with your permission. At the beginning of your radiotherapy you'll get instructions on how to look after your skin in the area being treated.

Before each session of radiotherapy the radiographer will position you carefully on the couch and make sure that you are comfortable. During your treatment, which only takes a few minutes, you'll be left alone in the room but you can talk by intercom to the radiographer, who will watch you from the next room. Radiotherapy is not painful but you have to lie still for a few minutes during the treatment.

Side effects of Radiotherapy Treatment

Radiotherapy can cause general side effects such as feeling sick (nausea) and tiredness. When radiotherapy is given to the head it can cause specific side effects such as severe tiredness and drowsiness (somnolence), which usually appear a couple of weeks after your treatment starts and may last for a few weeks.

Hair loss

If you have radiotherapy to the head or to the testes, the hair in these areas will fall out. This is only temporary and it will usually grow back once your treatment is over, but it may not be as thick as it was before.

Feeling sick

Nausea can usually be effectively treated by anti-sickness drugs (anti-emetics), which your doctor can prescribe. If you don't feel like eating, you can replace meals with nutritious high-calorie drinks. These are available from most chemists and can also be prescribed by your GP.

Tiredness

As radiotherapy can make you tired, try to get as much rest as you can.

All these side effects should disappear gradually once your treatment is over, but let your doctor know if they continue.

Radiotherapy does not make you radioactive and it is perfectly safe for you to be with other people, including children, throughout your treatment.

Our booklet on Radiotherapy gives more details about the treatment.

High-dose treatment with stem cell support for ALL

A stem cell transplant allows you to have much higher doses of chemotherapy than usual and may help to improve the chances of curing the leukaemia, or prolonging a remission.

Stem cells are blood cells in the very earliest stage of development in the bone marrow. They develop into the different types of blood cell.

High-dose treatment with stem cell support involves having very high doses of chemotherapy and sometimes radiotherapy over a few days. This destroys the bone marrow cells. After the treatment, stem cells, usually from either a sibling or unrelated donor, are given to you by a drip (infusion). These stem cells find their way to the bone marrow where they start producing new blood cells. This type of transplant is known as an allogeneic stem cell transplant.

Stem cell transplants may benefit a number of people with ALL. They are used to improve the chances of curing it or prolonging a remission, but may not be suitable for everyone. High-dose treatment is usually used after initial chemotherapy treatment.

If your specialist thinks that a stem cell transplant is necessary or a possible treatment option for you, they will discuss it with you in detail.

Other drugs

There are other drugs which can be used as part of the treatment for ALL. These are:

Dasatinib (Sprycel®)

Dasatinib is used in adults with Philadelphia chromosome positive ALL that is resistant to previous treatment, including imatinib. Like imatinib, dasatinib also works by blocking (inhibiting) the signals within the leukaemia cells that make them become abnormal and continue to divide. This makes the cells die.

While this drug is licensed for use in ALL, it hasn't been approved for use by NICE (National Institute for Health and Clinical Excellence) in England and Wales and so it is not generally available.

Nelarabine (Atriance®)

Nelarabine is a chemotherapy drug that is used to treat some types of ALL which have been resistant to treatment or come back after treatment. In Scotland, this drug has been approved for use before a stem cell transplant, but it is not generally available in the rest of the UK.

Rituximab (Mabthera®)

Rituximab is a drug which is being tested to see if helps in the treatment of some types of ALL.

It belongs to a group of drugs known as monoclonal antibodies which work by recognising a particular protein on the surface of leukaemia cells. By locking onto these proteins, it is able to destroy the leukaemia cells. Research into the use of rituximab in ALL is still ongoing and it's not yet generally available.

Steroid therapy for ALL

Steroids are often given with chemotherapy to help destroy the leukaemia cells.

Prednisolone or dexamethasone are two commonly used steroids for ALL.

Side effects of steroid therapy

Steroids for ALL are generally given only for a few days a month and so usually have few side effects. They are given as tablets. The side effects you may notice are a bigger appetite, feeling more energetic and difficulty sleeping.

If you take steroids for some time, you may have some other temporary side effects. These can include water retention, high blood pressure, indigestion and a slightly increased risk of getting infections.

You may also have an increased level of sugar in the blood. If this happens, your doctor will prescribe drugs which will need to be taken daily to bring your blood sugar level back to normal. You may have to do a simple daily test to check for sugar in your urine. Your nurses will show you how to do this.

It is unusual for people with acute lymphoblastic leukaemia to have to take steroids for a long time, but if you do you may notice that you put on weight.

It is important to remember that all these side effects are temporary and will gradually disappear as the steroid dose is reduced. You should carry a card with you, or wear a Medicalert, stating that you are taking steroids.

Imatinib (Glivec[®]) for ALL

Imatinib is a drug known as a tyrosine kinase inhibitor or signal transduction inhibitor which may be used as part of the treatment for people with Philadelphia chromosome positive ALL. Imatinib is taken by mouth as capsules.

It works by blocking (inhibiting) signals within the leukaemia cells that make them become abnormal and continue to grow and divide. Inhibiting the signals makes the cells die.

Imatinib may make you feel a bit sick, and sometimes causes diarrhoea. It may also cause leg aches and cramps, rashes, and swelling of the face, especially around the eyes. The side effects are usually mild and treatable.

Research - Clinical trials for Acute Lymphoblastic Leukaemia

Research trials are carried out to try to find new and better treatments for leukaemia. Trials that are carried out on patients are known as clinical trials.

Clinical trials may be carried out to:

- test new treatments, such as new chemotherapy drugs, gene therapy or cancer vaccines
- look at new combinations of existing treatments, or change the way they are given, to make them more effective or to reduce side effects
- compare the effectiveness of drugs used to control symptoms
- find out how cancer treatments work
- see which treatments are the most cost-effective.

Trials are the only reliable way to find out if a different or new treatment is better than what is already available.

Taking part in a trial

You may be asked to take part in a treatment research trial. There can be many benefits in doing this. Trials help to improve knowledge about leukaemia and develop new treatments. You will also be carefully monitored during and after the study.

Usually, several hospitals around the country take part in these trials. Bear in mind that some treatments that look promising at first are often later found not to be as good as existing treatments, or have side effects that outweigh the benefits.

If you decide not to take part in a trial, your decision will be respected and you do not have to give a reason. There will be no change in the way you are treated by the hospital staff and you'll be offered the standard treatment for your situation.

Blood and tumour samples

Many blood and bone marrow samples may be taken to help make the right diagnosis. You may be asked for your permission to use some of your samples for research.

If you're taking part in a trial you may also be asked to give other samples which may be frozen and stored for future use when new research techniques become available. These samples will have your name removed from them so you can't be identified.

The research may be carried out at the hospital where you are treated, or at another one. This type of research takes a long time, and results may not be available for many years.

The samples will, however, be used to increase knowledge about the causes of leukaemia and its treatment. This research will, hopefully, improve the outlook for future patients.

Living with ALL

What if ALL comes back?

In 5-6 out of 10 adults (50-60%) ALL comes back after a period of remission. This is called a relapse.

The ALL may come back in the bone marrow, the fluid around the brain and the spinal cord or, in men, in the testes.

If this happens further treatment can be given. For some people, the chemotherapy drugs used during the induction phase may be repeated. However, for others, their leukaemia may be resistant to these drugs, so different drugs or new combinations of drugs may be needed. Treatment with high-dose chemotherapy and stem cell support may also be recommended if it has not been given before. With further treatment about 1 in 3 people (33%) will have another remission.

Sometimes treatment will only be able to control the leukaemia. In this case the aim of treatment will be to reduce symptoms and improve quality of life.

Follow-up after treatment for ALL

Once your treatment is completed, you'll have regular check-ups and x-rays. These will continue for several years. If you have any problems, or notice any new symptoms between these times, let your doctor know as soon as possible.

Blood tests

Samples of blood will be taken regularly throughout your treatment to check your general health and the number of normal and abnormal cells in the blood.

How treatment for ALL may affect your fertility

Some of the drugs used to treat acute lymphoblastic leukaemia can cause temporary or permanent infertility. Your doctor will talk to you about this before you start your treatment. If you have a partner you may want them to join you at this time so you can discuss any fears or worries together.

Some drugs have less effect on fertility than others, and couples who have had normal, healthy babies after one of them has been treated for leukaemia. Unfortunately, people who have had intensive chemotherapy and radiotherapy and a stem cell transplant, are likely to be permanently infertile.

It may be possible for men to store sperm before starting treatment, so it can be used later if they want to have a family. Rarely, a woman's eggs or fertilised eggs (embryos) can be stored before chemotherapy, so that she may have the chance to have a child after treatment.

However, as treatment usually has to start as soon as possible, there is not always enough time to store sperm or embryos.

As your doctor knows the details of the treatment you are having, they are the best person to answer your questions. You can write down any questions that you have so you are clear about your treatment, and the effect it is likely to have on you, before it starts.

Coping with infertility

If chemotherapy has made you infertile, it can be difficult to come to terms with the fact that you cannot have children.

Talking about your feelings with your partner, family or a close friend can help to clarify your thoughts and give the people close to you the opportunity to understand how you are feeling.

If it would be easier to talk to someone outside the circle of your immediate friends and family, you may find it helpful to talk to your doctor, nurse, social worker or a trained counsellor.

We have more information about sexuality and cancer, as well as information on sex, relationships and fertility for young people affected by cancer.

Living with and after cancer

Cancer can affect many areas of your life such as your finances, work, your emotions and relationships. Find information and advice about what the effects might be, how to deal with them and how we can help.

Financial support

Find practical advice on the possible financial impact of a cancer diagnosis, including what benefits you might be entitled to.

Practical issues

Information on dealing with day-to-day problems, including work, travel, and travel insurance.

Emotional effects

Information on the emotions you might experience as a result of your cancer diagnosis, ways that you might manage them and other sources of support.

Relationships and communication

Advice on how to talk to other people, talking to children, relationships and sexuality.

NOTE: JASCAP has booklets on the above subjects.

Questions you might like to ask your doctor

You can fill this in before you see the doctor or surgeon, and then use it to remind yourself of the questions you want to ask, and the answers you receive.

1. _____

Answer _____

2. _____

Answer _____

3. _____

Answer _____

4. _____

Answer _____

5. _____

Answer _____

JASCAP : We need your help

We hope that you found this booklet useful.

To help other patients and their families we need and intend to extend our Patient Information Services in many ways.

Our Trust depends on voluntary donations. Please send your donation by Cheque or D/D payable in Mumbai in favour of "JASCAP".

Note for Reader

This JASCAP booklet is not designed to provide medical advice or professional services and is intended to be for educational use only. The information provided through JASCAP is not a substitute for professional care and should not be used for diagnosing or treating a health problem or a disease. If you have, or suspect you may have, a health problem you should consult your doctor.

JASCAP

JEET ASSOCIATION FOR SUPPORT TO CANCER PATIENTS,
C/O ABHAY BHAGAT & CO., OFFICE NO.4, "SHILPA",
7TH. ROAD, PRABHAT COLONY,
SANTACRUZ (East),
MUMBAI - 400 055.
PHONE: 91-22-2617 7543 & 91-22-2616 0007
FAX: 91-22-2618 6162,
e-mail: pkrijascap@gmail.com, abhay@abhaybhagat.com

AHMEDABAD: MR. D.K.GOSWAMY,
1002, LABH, SHUKAN TOWER,
NEAR JUDGES' BUNGALOWS,
AHMEDABAD - 380 015.
PHONE : 91-79-6522 4287. Mob : 93270 10529
e-mail : dkgoswamy@sify.com

BANGALORE: MS. SUPRIYA GOPI,
455, I CROSS,
HAL III STAGE,
BANGALORE – 560 075
PHONE : 91-80-2528 0309 .
e-mail : supriyakgopi@yahoo.co.in

HYDERABAD: MS. SUCHITA DINAKER & DR. M. DINAKER, M.D.,
FLAT NO. G4, 1ST. FLOOR, "STERLING ELEGANZA",
STREET NO.5, NEHRUNAGAR,
SECUNDERABAD – 500 026.
PHONE : 91-40-2780 7295.
e-mail : suchitadinaker@yahoo.co.in