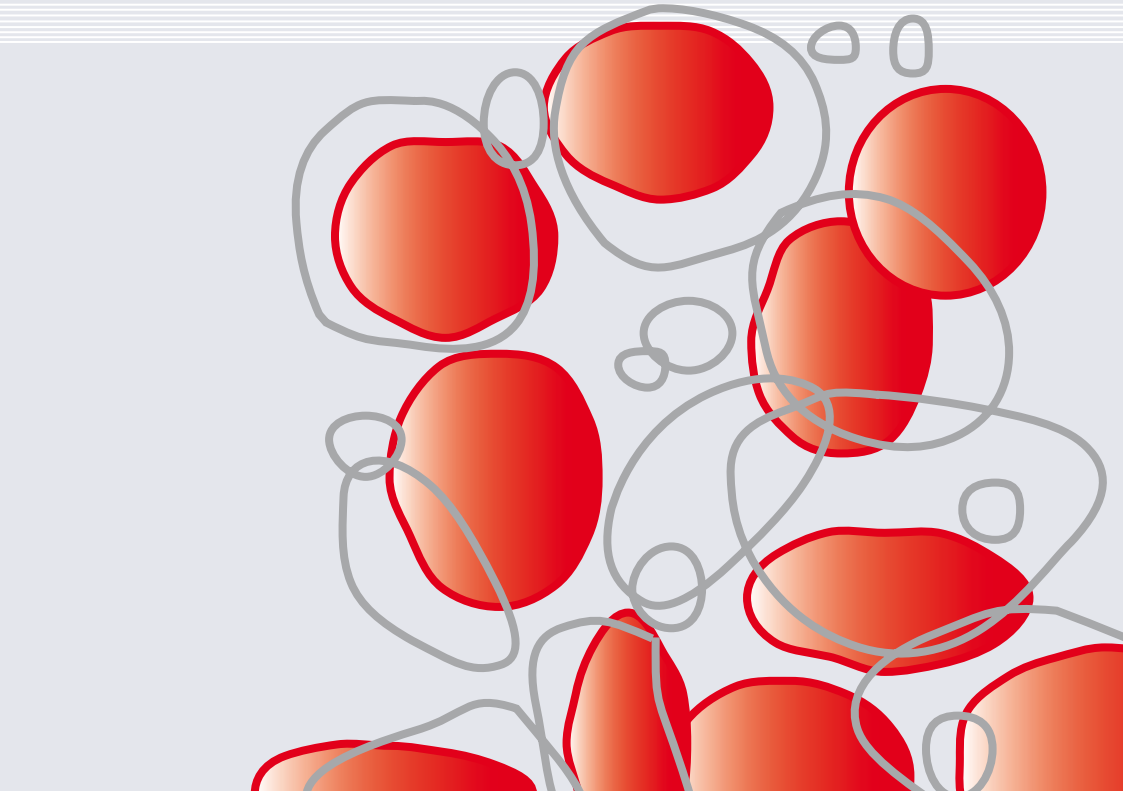
LEUKAEMIA RESEARCH

HODGKIN'S | LYMPHOMA | MYELOMA

Leukaemia and Related Diseases



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The diagnosis of a blood cancer can be a devastating event for patients, families and friends. It is therefore vital for everyone to have access to reputable and understandable information to help cope with the illness. Whenever possible our booklets are written in line with national guidelines for the treatment of patients with a blood cancer. The information in our booklets is more detailed than in many others but is written in a clear style with all scientific terms explained for the general reader.

We recognise that the amount and level of information needed is a personal decision and can change over time. Particularly at the time of diagnosis, patients may prefer less detailed information. A number of alternative sources of information are available which complement our publications.

The booklets in this series are intended to provide general information about the diseases they describe. In many cases the treatment of individual patients will differ from that described in the booklets.

At all times patients should rely on the advice of their specialist who is the only person with full information about their diagnosis and medical history.

For further advice contact the clinical information team on 020 7269 9060.

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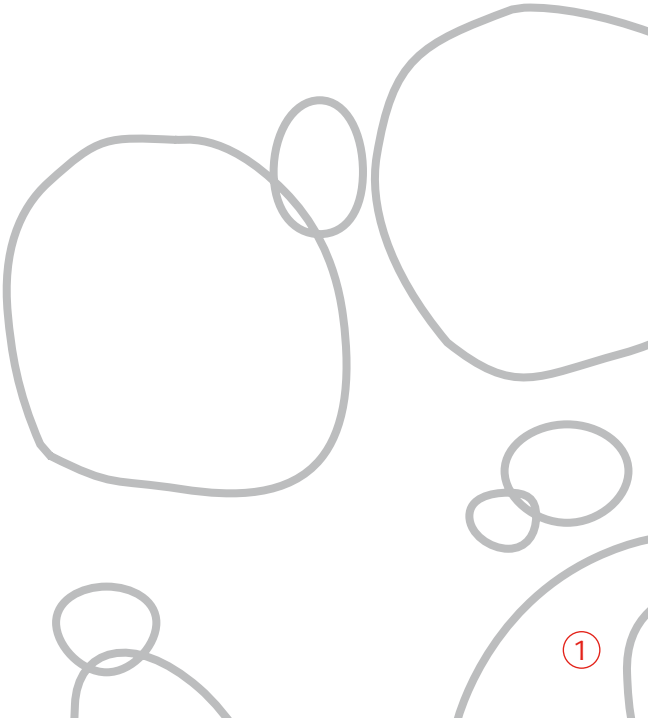
Series compiled by Ken Campbell, revised 2006. A list of advisors can be found at www.lrf.org.uk/advisors
The design of this booklet has been produced with kind assistance from Euro RSCG Life.

Leukaemia and related disorders are cancers of the blood. This handbook provides information about:

- Blood, bone marrow and the lymphoid system
- The signs and symptoms of blood cancers
- The diagnostic tests used for blood cancer
- The main forms of treatment

For the most current information available you are advised to visit the Leukaemia Research website at www.lrf.org.uk. Our website is regularly reviewed and updated.

This booklet and additional specialised publications on blood cancers and other diseases can be downloaded from the above website. Printed copies are available from Leukaemia Research.



The blood in health

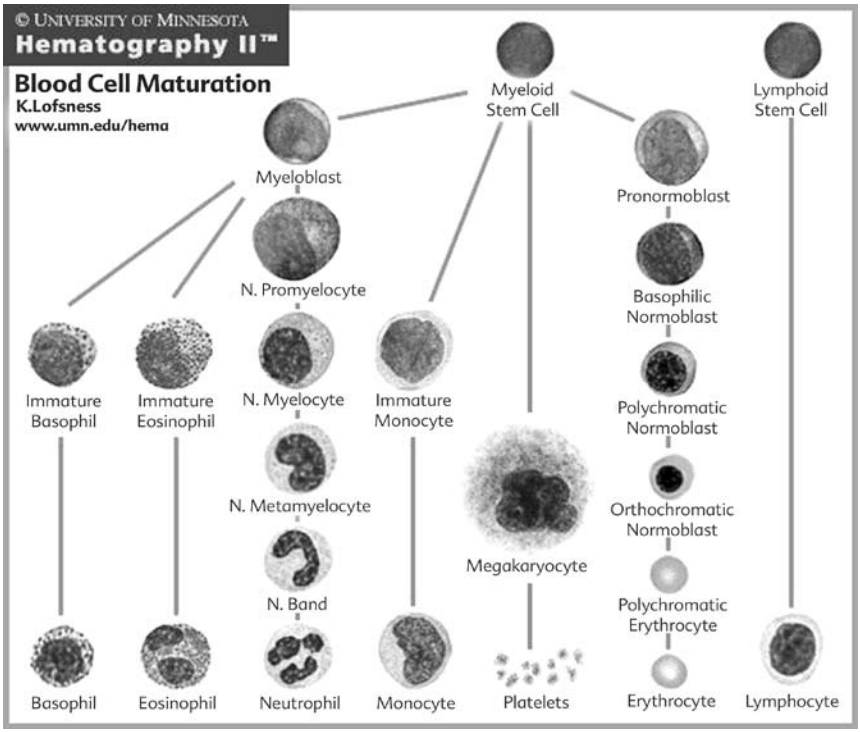
“Nature is nowhere accustomed more openly to display her secret mysteries than in cases where she shows traces of her workings apart from the beaten path. . .”

William Harvey (1578-1657)

Cells of the blood

Blood consists of a fluid (plasma) which contains three main types of cells; red blood cells (erythrocytes), white blood cells (leukocytes), and platelets (thrombocytes). The numbers of each type of blood cell vary between people and at different ages but are quite stable for healthy individuals. Each type of blood cell has different functions.

Red cells contain a pigment called haemoglobin, which can bind oxygen and carry it from the lungs to the tissues where it is released to fuel the body's chemistry. White cells are vital components of the body's immune system; its defence against invading organisms. The immune system consists of the white cells in our blood and a number of sites including lymph nodes, which are spread throughout the body, the spleen, tonsils, adenoids and other organs. There are several different types of white blood cell. The key components of these organs, called the lymphoid tissues, are large numbers of white cells called lymphocytes. Platelets form the first line of response to tissue injury, they stick together at the site of damage and stop the bleeding. They also release substances which trigger the formation of a firm clot, a scar and healing.



Origin of the different types of blood cells from bone marrow stem cells.

Blood cell production

All types of blood cell are made in the bone marrow which is a spongy tissue in the middle of bones. Blood cells are produced from very primitive cells called stem cells. Less than 1 in 5,000 of the marrow cells is a stem cell. The stem cells give rise to a progressively maturing series of different cell types which eventually lead to all the functional blood cells found in the circulation.

Growth and development of normal cells in the bone marrow is carefully controlled to produce the correct number of each type of cell to keep the body healthy. This is extremely demanding with about three million red cells and 120,000 white cells produced every second. The life span of blood cells varies widely. Red blood cells live for about four months after they leave the bone marrow, the most common white cell, the neutrophil has a life time of just a few hours and platelets of a few days. It is because white cells and platelets have such short life spans that they cannot easily be replaced by transfusions, although some specialised lymphocytes live for many years. To maintain the proper numbers of each type of blood cell it is important that cells die off and are cleared from the blood at the end of their useful life span. A blood cancer results either from a failure of cells to grow old and die or an excessive, uncontrolled production of cells, or more commonly, a combination of both factors.

Both the production of blood cells and maintenance of the correct numbers of each type of blood cell are controlled by chemicals called growth factors. These will be mentioned again under treatment as some growth factors have been produced in the laboratory and are now used in treatment. It is also known that abnormal levels of growth factors are involved in the actual disease process in some cases, for example patients with myeloma have abnormal levels of a growth factor called IL-6 in the blood and bone marrow.

The conditions

"Whatever State of the human Body doth disorder the vital, the natural, or even the animal functions of the same, is called a Disease."

Hermann Boerhaave (1715)

It is important to recognise that each patient is unique and their experience of their disease is equally unique. Any printed information is inevitably generalised. The only person who can offer reliable advice to a patient on how their disease might progress and how it might respond to treatment is their own doctor. Patients are entitled to ask for a second opinion (and many consultants recognise this and welcome such a suggestion) especially if the condition is a rare one or has presented in an unusual way. It should be emphasised that requesting a second opinion does not imply that a patient lacks confidence in their specialist. When someone has a serious, possibly life-threatening, illness it is natural that they wish to ensure they have sought all the advice available.

Leukaemia

The word leukaemia comes from a Greek word which means literally 'white blood'. Leukaemia is often referred to as cancer of the blood. The term refers to a group of closely related malignant conditions affecting the immature blood-forming cells in the bone marrow.

In leukaemia normal control mechanisms break down and the marrow starts to produce large numbers of abnormal white blood cells of an identical type. This disrupts the normal production of blood cells leading to anaemia and a low platelet count. Often in leukaemia the spleen and liver will become enlarged and this may cause abdominal discomfort. Also, in some cases, the lymph glands (described below) are enlarged. The large numbers of white cells

being produced in leukaemia are all abnormal which means that patients may have frequent, severe infections because the diseased white cells are being produced in place of normal, infection-fighting cells.

Leukaemia can be classified as lymphoid or myeloid and as either acute or chronic. Lymphoid and myeloid refer to the type of white cell affected. If this is a lymphocyte or lymphocyte-like cell, the condition is called lymphocytic or lymphoblastic leukaemia. Myeloid leukaemias affect any of the other types of white blood cells or the red cell or platelet producing cells (called megakaryocytes). The terms acute and chronic are often misunderstood. They refer only to the speed at which the disease progresses if it is left untreated, not to the severity of the disease. Acute leukaemia comes on quickly and, if not effectively treated, will rapidly progress. Chronic leukaemia is slow to develop and slow to progress, even when not treated.

Lymphoma

Lymphomas are cancers of the lymphatic tissues.

The lymphatic system is a series of fine vessels similar to blood vessels. It drains fluid away from the tissues and returns it to the bloodstream. Throughout the system there are small organs called lymph nodes (sometimes called lymph glands). There are clusters of nodes in the armpits, groins, neck and in the pelvis, abdomen and chest. In response to an infection the lymph nodes may become swollen. For example, the swollen glands that many people associate with a throat infection are really lymph nodes. They are packed with specialised white cells called lymphocytes. Lymphocytes also make up a significant proportion of the circulating white blood cells. Lymphocytes can be classified by special laboratory tests into B cells, T cells and null cells. These categories reflect their function; B cells are mainly responsible for production of antibodies, T cells control the behaviour of other lymphocytes and may be capable of killing some infectious organisms, especially viruses. One important group of null cells are the natural killer cells, which can kill infecting organisms and parasites directly.

The different types of lymphocytes are grouped within the lymph node in a very specific way according to their function. The spleen (an organ in the upper abdomen which helps fight infection and removes worn-out blood cells), the thymus (an organ under the breastbone) and the tonsils and adenoids (in the throat) are also part of the lymphatic system. There are localised areas of lymphoid tissue within the skin and in the gut wall. These can give rise to specific types of lymphoma. There are many different types of lymphoma but historically two main groups have been recognised. One group is called Hodgkin's lymphoma and the other is known as non-Hodgkin's lymphoma.

Multiple myeloma

Multiple myeloma is a form of cancer that affects a specialised type of lymphocyte called a plasma cell. Plasma cells are a specialised form of B-lymphocyte that normally produce antibodies. Multiple myeloma is the commonest of the plasma cell malignancies. Occasionally myeloma presents in just one site (plasmacytoma) or as a leukaemia-like illness (plasma cell leukaemia).[1]

Multiple myeloma is overwhelmingly a disease of later life. It is rare in young adults and unknown in children. The condition is called multiple myeloma because most patients have evidence of disease at a number of different bony sites in the body. The disease is accompanied by a breakdown in the structure of the bones. This is due to increased activity of cells in the marrow which continually break down and reform bone. In myeloma the destruction exceeds replacement and ‘holes’ in the bones result. This also releases large amounts of calcium into the blood which may lead to kidney damage. There are several stages of multiple myeloma. A high proportion of patients with myeloma will, at some stage during their treatment, become free of symptoms and require no active treatment. This occurs even though the disease has not been eliminated. This is known as plateau-phase and may last for several years.

[1] There are separate publications describing these forms of the disease available from Leukaemia Research.

Myelodysplastic syndromes

The myelodysplastic syndromes (MDS) are a group of diseases[2] in which the production of blood cells is severely disrupted. Myelodysplasia is a potentially confusing term that may be used either to describe certain abnormal features seen in the bone marrow or to refer to the specific condition MDS. If there is any doubt about which is meant, it is important for the patient to clarify with the specialist how the term is being used. In contrast to leukaemia, in which just one type of blood cell is produced in excessively large numbers, the production of any one and sometimes all types of blood cells may be affected in myelodysplastic syndrome. The poor quality of the blood cells produced means that a significant proportion of them are destroyed before they leave the bone marrow. This means that the levels of red cells, white cells and platelets in the blood may be abnormally low. When the levels of all types of blood cells are low the condition is called pancytopaenia.

Myelodysplastic syndrome is mainly seen in people over the age of 50 years and in this age group it is more common in men. In younger patients the numbers of men and women are about equal.

Treatment of myelodysplastic syndrome is not usually aimed at affecting the progress of the underlying disease but at improving quality of life by reducing and controlling symptoms of anaemia (due to lack of haemoglobin), infections (due to lack of white cells) or spontaneous bleeding (due to lack of platelets). This is known as supportive treatment.

The myeloproliferative disorders

The myeloproliferative disorders are a group of conditions in which there is overproduction of one or more type of blood cell. Polycythaemia rubra vera (PRV) mainly affects red blood cells, essential thrombocythaemia (ET) mainly affects platelets while in myelofibrosis there is excessive production of the fibrous tissue which normally acts as a support for the bone marrow.

[2] Refractory anaemia (RA), refractory anaemia with ring sideroblasts (RARS), refractory anaemia with excess blasts (RAEB), refractory anaemia with excess blasts in transformation (RAEBt) and chronic myelomonocytic leukaemia (CMML).

Aplastic anaemia

Patients with aplastic anaemia have a failure of production of all types of blood cells. The bone marrow contains large numbers of fat cells instead of the blood producing cells which would normally be present. This is called marrow hypoplasia or aplasia. The disease in most cases is acquired, that is it is not inherited and is not present from birth. Marrow hypoplasia is an inevitable consequence of the use of high doses of drugs and radiotherapy in the treatment of cancer. However, this type of bone marrow failure differs from acquired aplastic anaemia in that prompt recovery is expected when the drug or radiation treatment is stopped. There is a rare inherited form of the disease called Fanconi anaemia.

The disease may affect people of any age but it is seen most often in young adults and in people over the age of 60 years.

Causes of leukaemia and related diseases

“The predisposing causes of cancer are three, ...viz., age, parts, and hereditary disposition; perhaps climate...”

John Hunter (1728-1793)

Like all cancers, leukaemias and the related diseases arise as a result of changes in, or damage to, the genes which control cell growth, development and division. In most cases, no specific cause can be identified. There are certain factors known to increase the risk of developing leukaemia or one of the related diseases. Very occasionally, there is a clear cause as in the cases of leukaemia and myeloma seen in atomic bomb survivors.

Specific causes

Inheritance

There is no evidence that any form of blood cancer can be inherited. Even in the very rare cases of blood cancer being present at birth, the disease has developed as a result of cell damage which happened in the womb. Recent research has demonstrated that in many cases of childhood leukaemia the initial genetic damage (which will eventually lead to leukaemia) occurs before birth. The factors in the mother's environment which lead to this are not known although there is clear evidence that smoking and/or heavy drinking during pregnancy increase the risk of childhood leukaemia.

In the majority of cases of leukaemia and other forms of cancer, there is no evidence that relatives of the patient are at greater risk than anyone else, though there are some inherited conditions in which the risk of developing

cancer is increased. These conditions account for only a very small number of cases of blood cancer. If the same form of leukaemia occurs in more than one member of a family, it may be appropriate to consult a genetic counsellor. It should be possible to arrange this through your specialist.

It is thought that possibly 10% of cases of chronic lymphocytic leukaemia may be familial — there is a web site discussing this topic at www.icr.ac.uk/haemcyto/fcll/index.html. A small percentage of acute myeloid leukaemia cases may be familial — this is very uncommon.

Down's syndrome is associated with an increased risk of developing leukaemia.[3] Children with Down's syndrome often have a leukaemia-like blood picture which becomes normal without treatment. This suggests that one or more genes on chromosome 21 may play important roles in the normal development of blood cell production.

Age

In general, the risk of developing leukaemia or a related condition increases with age. With over three million new blood cells being produced every second, it is inevitable that some cells will accumulate damage to genes over the years. The only reason that cancer is not even more common with increasing age is that all cells in our body have quite sophisticated defences against harmful mutations. Usually, when cells undergo changes to their genetic material these are detected and the cell undergoes a form of suicide, called apoptosis or programmed cell death. There are a few types of blood cancer, however, which occur more commonly in childhood than in adults. One of these is acute lymphoblastic leukaemia, which is more common between the ages of two and five years than at any other age. This is known as the childhood peak of leukaemia. Some diseases, such as myeloma and chronic lymphocytic leukaemia, are extremely rare in young people.

[3] There is a separate publication on Down's Syndrome available from Leukaemia Research.

Infections

Leukaemia is not a condition that can be acquired by contact with a person who has the disease. It is however possible that some viral infections may act as triggers or as co-factors. The pattern of exposure to infection may explain the childhood peak of acute lymphoblastic leukaemia. As the level of childhood infectious disease has declined in developed nations and families have become smaller, it has become less common for children to be exposed to infection(s) in the first year of life. Rarely, a delayed first stress on the immune system may lead to the development of leukaemia. Evidence to support this includes a reduction in risk for leukaemia seen following some types of immunisation and in children who attend crèches or similar groups during the first year of life.

The population mixing that occurs when a new town is built or large numbers of workers move into a new area has also been suggested as a significant cause of childhood leukaemia. In this case the stress is less on the timing of exposure and more on the novel nature of the infectious agent. This theory and the timing of infection theory are not exclusive; it is likely that both factors influence the risk of developing leukaemia.

There is only one virus definitely known to cause leukaemia or lymphoma in humans. This virus is called HTLV-1 (human T cell leukaemia/lymphoma virus). It is only common in Japan and to a lesser extent in the Caribbean. It takes decades from the time of infection for the leukaemia or lymphoma to develop. This virus causes very few cases of leukaemia or lymphoma seen in the UK.

A virus called the Epstein-Barr virus (EBV) is associated with some cases of a type of lymphoma called Hodgkin's lymphoma in children and older adults. It is clear that EBV by itself is not enough to cause the disease because infection with the virus is very common in the general population whereas Hodgkin's lymphoma is fairly rare.

There are no other definitely identified links between a virus and leukaemia or lymphoma but some experts believe that other forms of the disease(s) may be caused by an abnormal reaction to an immune stimulus, possibly from a virus.

Aplastic anaemia, which is a rare disease, may occur as a complication of viral hepatitis or of other viral infections. Viral infections are, however, probably the cause of only a very small number of cases.

Chemicals

The commonest chemical exposure linked to leukaemia is almost certainly cigarette smoking; which has been shown to be a significant risk factor for acute myeloid leukaemia. It has been estimated that as many as a quarter of all cases may be caused by smoking. Benzene in high concentrations is known to cause leukaemia and it is possible that other similar chemicals may increase the risk of leukaemia and related diseases. The major source of benzene exposure in the UK population is cigarette smoke. Some people are exposed to benzene in the course of their work. There are very strict regulations governing the use of benzene in the workplace and it is very unlikely that anyone in Britain would be exposed to dangerous levels of benzene because of their occupation. There are very small amounts of benzene present in unleaded petrol but this is not considered high enough to be a leukaemia risk.

In some groups of workers, for example farmers and agricultural workers, there appears to be an increased risk of certain conditions, such as myeloma and lymphoma. This may be related to chemical exposures but there are many other features of an agricultural lifestyle which might be responsible including chronic exposure to pollen and other biological material which might stimulate the immune system.

Radiation

Ionizing radiation

Ionizing radiation is the term used for the kind of radiation given off by X-ray machines or by radioactive materials. High doses of radiation can definitely increase the risk of leukaemia and related diseases. This has been shown in the atomic bomb survivors and by the experience of other people accidentally exposed to high levels of radiation. Most experts believe it is extremely unlikely that very low levels of radiation can cause leukaemia or related diseases. Very few, if any, people in Britain are likely to be exposed to the high levels of radiation which are known to cause leukaemia.

Some years ago it was reported that children who had been exposed to medical X-rays before birth were more likely to develop leukaemia. The introduction of ultrasound has virtually eliminated the need to use X-rays during pregnancy. Special care is taken by hospital staff to avoid X-raying women who might be pregnant. Modern X-ray machines deliver a much smaller dose of radiation. On the very rare occasions when a pregnant woman needs to be X-rayed, special precautions are taken to reduce the risk even further.

Non-ionizing radiation

Some studies have suggested that there appears to be an increased risk of leukaemia in children who live near electrical power-lines or other electrical facilities. It is suggested that electromagnetic fields (EMF) may be capable of either causing leukaemia or accelerating the development of the condition. These studies have relied on very small numbers of cases and on estimates of the strength of exposure to electromagnetic fields. The majority of published reports have concluded that it is very unlikely that there is any increase in the risk of leukaemia as a result of exposure to electromagnetic fields. The use of electricity has increased enormously over the last 20 to 30 years whilst the rate of childhood leukaemia has remained relatively constant. The peak in the number of childhood cases between two and five years of age cannot be explained by this theory.

A consortium of UK cancer charities has funded the largest ever study of possible causes of childhood cancer. One aspect of this study has been to consider the possibility that proximity to overhead power lines or other electrical facilities might increase the risk of childhood leukaemia. The results of this study have shown no evidence in the UK of any relationship between proximity to power lines and the risk of childhood leukaemia. The majority of large studies in other countries have confirmed similar negative results.

A recent report indicated that there may be an association between very high magnetic fields (more than 0.4 micro Tesla) and a slight increase in risk of childhood leukaemia. The report stressed, however, that this association did not prove that exposure to powerlines caused leukaemia. Importantly, the report emphasised that only about 0.5 % of children in the UK would be exposed to such high intensity fields.

Secondary leukaemia

Some forms of leukaemia and related diseases are seen more often than is usual in patients who have received intensive therapy with anti-cancer drugs. This is known as secondary leukaemia. The most common conditions seen in this group of patients are acute myeloid leukaemia and myelodysplastic syndrome. It is important to understand that only a very small percentage of cancer patients go on to develop leukaemia or a related condition as a result of their treatment. Unfortunately, these secondary malignancies are often more resistant to drug treatment and may be very difficult to treat.

There are two major types of treatment-related AML. One type, which follows treatment with alkylating agents, tends to come on within five to ten years after treatment, often is preceded by MDS and is associated with characteristic chromosome changes. The other type results from treatment with a class of drugs called topoisomerase II inhibitors — there is usually only a short delay after treatment, the condition presents as myelomonocytic or monocytic leukaemia (rather than MDS) and the chromosome changes are different.

Diagnosis

"Observe, record, tabulate, communicate. Use your five senses. It is much more important to know what sort of a patient has a disease than to know what sort of a disease a patient has."

William Osler (1849-1919)

Signs and symptoms

In leukaemia and related diseases the signs and symptoms of illness are non-specific. The features may be different in the different types of leukaemia. These signs and symptoms can all occur in more common, non-cancerous conditions. For example, most patients with brain tumours will have headaches at some time but very few headaches are caused by brain tumours. Patients may show any combination of symptoms. Some may be more obvious than others. Initial symptoms may appear to be nothing worse than a bout of flu. Anyone who develops persistent symptoms should see their doctor promptly.

The symptoms which are seen most often in leukaemia and related diseases are:

- Fatigue and limited capacity for exercise
- Breathlessness on exertion
  - Paleness, tiredness, weakness, or fatigue and breathlessness are caused by anaemia (low haemoglobin[4] levels which reduces the ability of the blood to carry oxygen)
- Excessive bruising, often spontaneous
- Bleeding from mucous membranes (gums, etc.) and from the gut; pre-menopausal women may have heavy menstrual bleeding
  - These symptoms are caused by a low number of platelets.

[4] Haemoglobin is the pigment in red blood cells which carries oxygen from the lungs to body tissues.

- Persistent infections
- Fever, which is often present even in the absence of clear indications of infection
- Night sweats
  - These are caused by low numbers of normal white blood cells and by a high metabolic rate. Infections are a problem because there are few normal white cells present. Fever may occur even in the absence of infection, probably as a result of a general speeding up of body metabolism because of the high rate of tumour cell production. This may also explain the night sweats that are typically a feature of lymphoma and some forms of leukaemia.
- Abdominal discomfort
- Feeling of fullness when eating
  - These may be a problem in those conditions where there is swelling of the spleen, the liver or both.
- Enlarged lymph nodes
  - Swollen lymph nodes are a particular feature of lymphoma but they may also be present in chronic lymphocytic leukaemia or acute lymphoblastic leukaemia.

In patients with multiple myeloma there are additional signs and symptoms.

- Pathological fractures
- Pain in bones
  - These are caused by bone lesions. Abnormal blood cell production in the bone marrow or damage to the bone in myeloma may cause the pain and lead to pathological fractures, that is broken bones resulting from very slight injuries.

Diagnostic tests

In most cases of leukaemia or related diseases the initial diagnosis is made at a local (District General) hospital. It is often necessary, depending on the exact diagnosis, for patients to be referred to specialist centres for treatment. Once initial treatment is complete many patients continue their treatment under the care of their local hospital; this is known as shared care.

Initial tests

These are carried out at the time of diagnosis or shortly afterwards.

Full blood count

This is a test which measures the different types of blood cell and the haemoglobin level. The full blood count is done on a machine. When a patient has leukaemia or a related condition this is usually clear from the initial results. These results may even indicate the most likely specific diagnosis. If the blood count shows clear abnormalities suggesting the possibility of leukaemia or a related condition, the general practitioner will be contacted urgently by the laboratory where the test has been done. A repeat blood count will be done (to confirm the result) and further tests will be arranged. A patient with leukaemia is likely to have a low red cell and platelet count and be anaemic. The total white cell count is usually much higher than usual. Most of these white cells, however, are immature and are incapable of fighting infections. This means that patients are prone to infection. In the acute leukaemias the white count may occasionally be lower than normal values.

Polycythaemia rubra vera will cause a very high haemoglobin level, red cell count and a high packed cell volume (PCV). The PCV is a measure of what proportion of the total blood volume is made up by the red blood cells. Patients with essential thrombocythaemia have very high platelet counts. The white cell count may be normal or reduced.

In patients with aplastic anaemia all the types of blood cell i.e. red cells, white cells and platelets, will be reduced.

Blood film report

If the results of a full blood count are abnormal, a blood film will be examined under the microscope. The appearance of leukaemia and many of the related diseases on a blood film is quite distinctive and the diagnosis is often clear by this stage. The blood count and blood film reports are of less significance in lymphoma and multiple myeloma, in which they often appear normal. In some cases of acute leukaemia, especially in children, the blood count and film may be normal or even show reduced numbers of cells.

Additional tests

These are carried out to confirm the diagnosis and may be repeated throughout the treatment and afterwards in order to monitor progress.

Bone marrow aspirate/biopsy

A bone marrow sample is necessary in almost all patients with leukaemia or a related disease. This involves obtaining a small amount of marrow from inside the bone with a needle, and usually a sample from the bone itself to show the structure of the bone marrow cavity. The first is known as a bone marrow aspirate, the second is a bone marrow trephine. The samples are usually obtained from the back of the hipbone, although rarely the sternum (breastbone) may be used instead for bone marrow aspirates (but not for trephines). The procedure causes some discomfort but does not take very long. The procedure is carried out with a local anaesthetic and in some cases sedation. In children, it is quite common for a general anaesthetic to be given.

Elderly patients with chronic lymphocytic leukaemia who are well at the time of diagnosis often need no treatment initially and they may not need to have a bone marrow biopsy. If treatment is required later, a biopsy will often be taken before treatment begins.

Chromosome analysis (karyotype)

This may be done on cells from the blood, the bone marrow or both. In leukaemia and related diseases there are changes to the chromosomes of the affected cells compared to normal cells from the same patient. The exact pattern of these changes may be important in diagnosing the exact type of leukaemia and in predicting the likely response to treatment. In some conditions, these changes may also allow the use of very sensitive tests to determine how well the disease is responding to treatment.

Diagnostic imaging

This may be carried out at various stages. Some patients will have none of the following tests were as some may have them done repeatedly.

eX-ray or radiograph

Most patients with leukaemia will require X-rays even if these are only chest X-rays to screen for infection. Some patients will require frequent X-rays. Patients may worry about this because they associate radiation with cancer but this should not be a concern. Modern diagnostic X-ray equipment gives very low doses of radiation and the benefit to the patient heavily outweighs any possible risk.

CAT scan or CT scan

This is a special form of X-ray examination. A series of X-ray pictures are taken very rapidly by a machine. A sophisticated computer then builds up the information into a 3-D picture of the internal organs that can be examined ‘slice-by-slice’. This overcomes the problem with conventional X-rays of difficulty in seeing soft tissues within the body. This is of particular importance when soft tissues would normally be obscured by shadows from bones.

MRI scan

MRI scans do not use X-rays. This form of imaging uses very strong magnets and reveals much more detail of soft tissues such as the brain and can detect infiltration by tumour. MRI scanning is very accurate in picking up multiple myeloma and lymphoma.

Classification, staging and prognostic stratification

"The urge to classify is a fundamental human instinct; like a predisposition to sin, it accompanies us into the world at birth and stays with us to the end."

Hopwood, A. T.; Proceedings of the Linnaean Society of London (1957)

Classification

The value of classification of the diseases is that in virtually all the main forms of blood cancer there appear to be biologically different subtypes of disease. These subtypes probably have different causes and in many cases respond differently to treatment. In some instances, the information used to classify the diseases is also important in predicting the likely response to treatment and prognosis. There are a number of systems for classifying the leukaemias and related diseases. These are based on morphology (the appearance of cells/tissues) and immunological and cytogenetic investigations.

In all forms of leukaemia, lymphoma and related diseases the initial diagnosis and classification is based on the morphology of the tumour cells as seen under the microscope. In the acute leukaemia and myelodysplastic syndromes morphological classification is based on a convention called the FAB system. This is described after the group of French, American and British haematologists who designed the scheme.

There are separate FAB classifications for acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML) and some conditions related to leukaemia. The ALL FAB classification is not widely used in clinical practice.

Management of L1 and L2 ALL is essentially the same and the L3 type is so different that it is treated more like a lymphoma than like other types of ALL. There are eight subtypes of AML in the FAB system. The most important of these in relation to treatment and outlook are listed below.

	FAB types of AML
M3	Also known as acute promyelocytic leukaemia. This form of the disease is usually very responsive to vitamin A derived drugs.
M6	This is also called erythroleukaemia because many of the leukaemia cells appear to be immature red cells rather than white cells.
M7	This form of AML affects the cells which make platelets.

The FAB classification of the myelodysplastic syndromes is:

- Refractory anaemia
- Refractory anaemia with ring sideroblasts
- Refractory anaemia with excess blasts
- Refractory anaemia with excess blasts in transformation
- Chronic myelomonocytic leukaemia

Immunological classification is mainly applicable to lymphoid malignancies; it is based on the type of lymphocyte affected, i.e. the B cell or the T cell. The immunological classification, together with the level of development in the T or B cell series, and the characterisation of chromosome abnormalities is extremely useful in predicting the response to treatment.

Lymphomas are classified according to a number of features including the appearance of the affected tissues under the microscope, the results of immunological tests and various specialised staining methods. In the past, a number of different classification systems have been in use. This caused great difficulty for clinicians and researchers in this field. As a result a classification called the Revised European American Lymphoma (REAL), which is more clinically and practically useful, was introduced. The REAL classification has now been adopted, with minor modifications, by the World Health Organization. This is called the REAL/WHO classification.

Occasionally patients are reclassified from a diagnosis of leukaemia to lymphoma or the other way around. This may seem alarming, implying uncertainty on the part of the doctors. In fact, lymphoma and lymphoid leukaemias represent extremes of a spectrum. In cases in the middle of this spectrum the diagnosis may depend on the specialist's opinion. This should not be a cause for alarm because in these borderline instances the treatment is the same however the condition is classified.

Staging

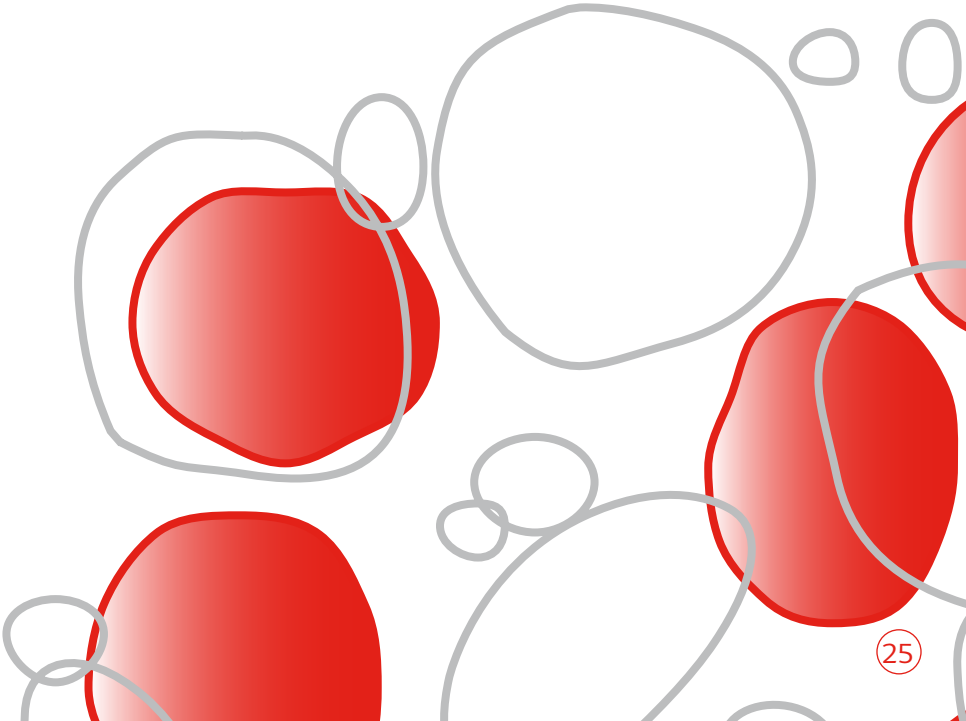
Staging is a system of estimating how extensively a disease has progressed from its starting point and whether the patient is showing significant symptoms. It is not used for acute leukaemia because the disease is usually widespread throughout the body and patients typically have symptoms of their illness when they are diagnosed.

In chronic lymphocytic leukaemia many patients are diagnosed by chance at a time when they feel perfectly well. The staging system for this disease is based on whether the lymph glands and spleen are enlarged as well as on the results of laboratory tests.

The staging system for lymphoma depends on the extent of spread of the disease and on what signs and symptoms the patient may have. For myeloma it depends not on the extent of spread but on the results of various tests which, taken together, indicate the severity of the disease.

In most other conditions related to leukaemia decisions on prognosis and on treatment are based on the classification of the subtype rather than on a staging system. In some diseases there are accepted methods for predicting which patients are likely to have good or less good outcomes.

These predictions are based mainly on the results of laboratory tests, although age and general health also have to be considered. This process is known as prognostic stratification. The exact number of categories and the way in which patients are assigned to categories vary widely between the different diseases.



Treatment

"Do not waste time and annoy the patient by doctoring a symptom; attack the disease."

Charles Warrington Earle (1891)

General principles

The different types and subtypes of leukaemia and related diseases vary greatly in their response to different forms of treatment. Some forms of the diseases are chemosensitive which means they are easily treated with chemotherapy (anti-cancer drugs). Similarly, forms of the diseases that are very responsive to radiotherapy are known as radiosensitive. If a patient has no response to treatment, their condition is described as refractory or resistant.

The primary objective of treatment is to eliminate all detectable tumour cells. This is called a remission. A complete remission occurs when the patient is symptom-free and laboratory tests show no evidence of malignant cells. Sometimes this will mean that the disease has been completely eliminated and the patient is cured. However even the most sophisticated tests cannot detect very small numbers of tumour cells and patients who are in complete remission, according to all available tests, may still have tumour cells present. Frequently a patient responds to treatment but there is still evidence of the disease; this is called a partial remission or partial response. If a patient has achieved either a partial or a complete remission but the disease later returns this is called a relapse. In some cases relapse occurs while the patient is still receiving active treatment. This is a relapse 'on-treatment' and often indicates that the malignant cells are resistant to the drugs or other treatment being used. This is often very difficult to treat although it may respond to the use of new drugs, particularly when these attack the malignant cells in a different

way to those already used. In other cases the condition relapses after all the active treatment has been completed. This is a relapse 'off-treatment'. Relapses off-treatment may occur because not all of the malignant cells have been killed when treatment is stopped. When this happens further treatment using the same drugs that were used to achieve the original remission may be successful.

Some patients may have very few symptoms and very slowly progressing disease, for example some older patients with chronic lymphocytic leukaemia. If this is so, the advice will often be that no treatment is necessary. However, the patient should have regular check-ups so that treatment can commence if the disease becomes more active. In other cases, such as some forms of myelodysplastic syndrome, the patient may be anaemic and have symptoms but there may be no treatments available which affect the course of the disease. In this situation treatment can be offered to control the symptoms and this may be referred to as supportive treatment or palliative therapy.

Chemotherapy

The mainstay of treatment for leukaemia and related conditions is the use of anti-cancer drugs (chemotherapy). Most anti-cancer drugs act by killing all dividing cells. Although this is effective against the cancer it also causes side-effects by damaging dividing cells, e.g. in the hair roots, skin and gut. There are some drugs that are more specific in killing the tumour cells and these tend to have fewer side-effects. For some types of leukaemia it is usual to use combinations of drugs to reduce possible problems of resistance that may otherwise develop. A specialised form of chemotherapy called biological therapy uses versions of natural substances such as interferon or growth factors which are produced in the laboratory. A new generation of drugs is emerging which are designed to target particular characteristics of the leukaemia cell. An example is Glivec (imatinib), which is now recommended as the standard choice for first-line treatment of chronic myeloid leukaemia.

Radiotherapy

Radiotherapy uses high energy X-rays to kill tumour cells. It is not normally used in leukaemia because the tumour cells are spread throughout the body and radiotherapy would give an unacceptably high dose of X-rays to healthy cells. It has been used in the past to kill acute lymphoblastic leukaemia cells in the fluid around the brain and spinal cord (where drugs cannot easily penetrate), but this use is becoming infrequent in children. Reduction in use of radiotherapy to the central nervous system (CNS) has been achieved by finding better ways to use existing drugs. Radiotherapy is mainly used in the treatment of lymphoma and in some of the plasma cell malignancies such as multiple myeloma and solitary plasmacytomas. It was thought that radiotherapy worked mainly by directly killing cells. It is now known that radiotherapy causes severe damage to the dividing cells without killing them. Such damaged cells normally self-destruct in a process called programmed cell death or apoptosis. The degree of radio-sensitivity of a particular type of blood cancer depends on whether the cells are still liable to die off if damaged. In some cancer cells damage to the genes that cause injured cells to self-destruct makes them resistant to radiation. Radiotherapy is just as non-selective as chemotherapy but, because it is possible to aim the radiation beam accurately, the side-effects tend to be more localised. Total body irradiation may be used in bone marrow/stem cell transplantation to prevent the recipient's immune system from rejecting the donor's stem cells.

Stem cell transplantation[5]

Stem cells from the bone marrow or blood are necessary to restore normal blood cell production when the bone marrow no longer functions. Sometimes damage to the bone marrow is the result of intensive treatment for leukaemia or a related cancer of the blood, in which case the patient requires a stem cell transplant. The most common reason for a transplant is treatment of leukaemia or other blood cancers, when these have a poor chance of being cured with conventional treatment. The most important aspect of the stem cell transplant is to provide enough of the stem cells that produce all the blood

[5] There is a separate publication on bone marrow and stem cell transplantation available from Leukaemia Research.

cells. It is also important to avoid complications of this treatment such as infection and rejection of the transplant.

Sources of stem cells

Stem cells may be obtained either from the bone marrow or by using a special machine to separate them out from the circulating blood. A transplant using stem cells obtained from the blood is called a peripheral blood stem cell transplant. In either case the stem cells may be those of the patient or from a donor.

An exciting development in the field of paediatric haematology is the use of stem cells from the umbilical cord blood of a newborn infant. It is hoped that tissue matching will be less of a problem using cord blood stem cells. These cells can be frozen and stored which offers the possibility of 'off-the-shelf' transplants. There is limited experience in the use of cord blood stem cells for adult recipients. The major problem is the comparatively low number of stem cells available in cord blood donations.

Types of donor

Transplants may be performed using the patient's own stem cells. This is called an autograft. Any form of transplant from a donor is called an allograft. If a family member of the patient provides stem cells they are known as a related donor. The best match in terms of tissue typing is an identical twin. This is called a syngeneic transplant. However, an identical twin may not be the ideal donor because there may be a higher risk of the original cancer returning.
The most common related donor is a tissue matching brother or sister of the patient, but occasionally a parent or child of the patient may be suitable. This form of transplant is only feasible for about one in three patients who have a sibling or, rarely, a parent with a matching tissue type. Less closely related kin are rarely a match so they are not usually tested. If no related donor is available, it may be necessary to seek a matched unrelated donor.

There are over nine million registered potential bone marrow donors worldwide. An increasing number of bone marrow transplants involve unrelated donors. The chance of finding a suitable matched unrelated donor is between one in 10,000 to 20,000. Patients who are not of Caucasian origin may experience greater difficulty in finding an unrelated donor. This is because tissue types vary in their frequency between different ethnic groups and the overwhelming majority of potential volunteer donors are Caucasians. For this reason donor registries are particularly anxious to recruit more volunteers from the ethnic minority communities.

Eligibility for transplantation

All transplants, whether donor or autologous, carry certain risks and the general physical condition of a patient is a key factor in determining whether they are eligible. The general health criteria are more strict for a matched donor transplant than for an autologous transplant. Until very recently this was reflected in a lower maximum age limit for donor transplants. A new technique, variously called a reduced intensity conditioned, mini-transplant or non-myeloablative transplant,has extended the range of availability of donor transplants. The key factor in the new technique is that it uses less intensive preparation with drugs and radiation.

Splenectomy[6]

A splenectomy may be performed in any form of blood cancer in which a very enlarged spleen is causing symptoms. The benefits of removing the spleen (splenectomy) vary depending on the degree of enlargement of the spleen and the exact nature of the disease. Splenectomy will, at the least, relieve the discomfort resulting from an enlarged spleen. In patients who have had their spleen removed there is a higher risk of certain types of serious infection. The risk is not so great that patients need to change their lifestyle but they should see a doctor immediately if they become ill and they must inform the doctor that they have had a splenectomy. They will be immunised against certain infections and take penicillin for life to reduce the risk of infection.

6 There is a separate publication on splenectomy available from Leukaemia Research.

Clinical trials[7]

A newly diagnosed patient is very likely to be invited to take part in a clinical trial. Clinical trials are carefully supervised comparisons of treatments to determine the best possible options. The starting point for a clinical trial is the best currently available treatment. The most common aims of a trial are to find out whether a new drug or a new way of using existing drugs might give improved results.

Clinical trials are an absolute requirement for the advancement of treatment for the blood cancers. The best available treatment can only be replaced by one that is compared against it and shown to be superior. There are three types of trial to evaluate either a new drug or clinical target for an already licensed drug. Phase I trials primarily focus on safety to establish how much of a new drug can be given to patients without causing serious adverse effects. Phase II trials involve small groups of patients to establish the best response to different doses and frequency of administration of a drug or combination of drugs. Phase III trials compare the effectiveness of the new drug (or combination with existing drugs) with the best available treatment to date. Most phase III trials are called randomised controlled trials because patients are allocated at random to one of the treatment arms. Any patient invited to join a trial will have a clear explanation from their doctor of what is involved. Any patient can refuse to enter a trial or withdraw at any time without any prejudice to the quality of their care. Most drug treatment (chemotherapy) is given according to treatment plans called protocols. Protocols stipulate which drugs should be used, the range of dosage and the timing of the drugs. If a patient is taking part in a clinical trial then they will definitely be treated according to a set protocol. Protocols are usually known by names derived from the initials of the drugs included. An example is CHOP which may be used in the treatment of lymphoma. The initials stand for cyclophosphamide, hydroxydaunorubicin, Oncovin (which is another name for vincristine) and prednisolone.

[7] There is a separate publication on clinical trials available from Leukaemia Research.

Types of drugs used in the treatment of leukaemia and related diseases

All anti-cancer drugs must be used with extreme caution, if at all, in patients who are pregnant or breastfeeding. Men and women who are on treatment are advised to take contraceptive precautions. Your specialist will give advice on how long these must continue after completion of treatment. Some forms of anti-cancer treatment may impair fertility. Patients who are hoping to have children after treatment must discuss the options to preserve fertility or store semen with their specialist.

Side-effects of medication often depend on the dosage being administered and on what other medical conditions a patient may have. It is preferable that advice on side-effects is given by a patient's specialist. Information on specific drugs can be obtained from the Electronic Medicines Compendium website, which can be accessed at http://emc.medicines.org.uk

Diet and leukaemia

There is no evidence that any special diet can influence the progress of leukaemia or any related condition. Patients should seek to ensure that they have a healthy balanced diet. If patients have no appetite, or are having difficulty eating, the hospital dietician may be able to offer advice. There are no foods which must always be avoided, unless a doctor advises otherwise. Alcohol, in moderation, is usually permitted except where it may interact with certain drugs. Some patients with lymphoma find that they become intolerant of alcohol by either becoming very sensitive to small quantities or even experiencing unpleasant reactions when they drink.

Vitamin supplements have not been shown to have any effect on the disease in normal amounts. Laboratory experiments have shown that some cancer cells grow better in the presence of very large amounts of Vitamin C. It is probably unwise to take very large dosages of any vitamin or other dietary supplement unless advised by your doctor to do so.

Patients who have a low white cell count may be advised to modify their diet to minimize the risk of infection.

Alternative and complementary therapies

Alternative therapies in this context mean treatments used in place of conventional treatment and complementary therapies mean treatments used alongside conventional treatment.

There are many extravagant claims made for alternative therapies, none of these has ever been substantiated and many patients have lost their lives as a result of rejecting conventional treatment. Anecdotal claims for cures in cases where patients have also received conventional treatment should be regarded with particular caution. Most treatments do not have their maximum effect immediately and it is common for patients to credit the most recent therapy with any improvement. Warning signs of 'quackery' include claims that a given treatment will cure many different diseases (with widely differing causes and natures), claims that a treatment cures all forms of cancer and claims that a treatment will cure cancer and AIDS.

Complementary therapies, such as aromatherapy and other massage therapies may offer significant quality of life benefits. There is no evidence that they affect the underlying disease process. Massage therapies should be undertaken with care by patients with lymphoma. Although it may be perfectly safe there is a theoretical risk that massage might force tumour cells into the circulation. Patients should check with their doctors before undertaking complementary therapies. The Bristol Cancer Help Centre (0845 123 2310) can offer information and advice on complementary therapies for cancer patients.

Summary

All of the conditions discussed in this booklet affect the bone marrow or the lymphoid system. The behaviour of the diseases is very different. Some of the conditions would be rapidly fatal if not treated whereas others are compatible with a long survival even without treatment. The severity of symptoms is very variable. Some patients, for example those with chronic lymphocytic leukaemia, may have no symptoms at the time of diagnosis. When symptoms are present they may resemble a bout of flu or other minor illness.

In most cases the cells affected are part of the immune system which means that patients are very susceptible to infection. Other symptoms depend on how badly the bone marrow is involved and on the direct involvement of other organs or tissues. If the spleen or liver are swollen this may cause abdominal pain. If the bone is affected, particularly in myeloma, then there may be quite severe bone pain.

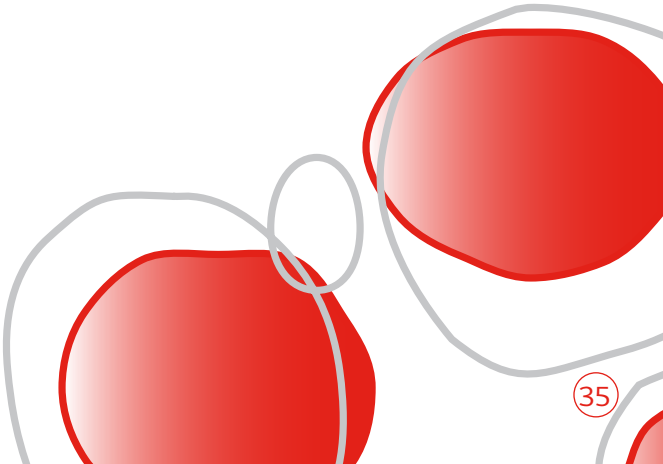
The only person who can offer reliable advice to a patient on how their disease might progress and how it might respond to treatment is their own doctor. Patients are entitled to ask for a second opinion and many consultants recognise this and welcome such a suggestion, especially if the condition is a rare one or has presented in an unusual way.

It is important to emphasise that requesting a second opinion does not imply that a patient lacks confidence in their specialist. When someone has a serious, possibly life-threatening, illness it is natural that they wish to ensure they have sought all the advice available.

Additional information

It may be helpful for patients or relatives to seek information from other patient support organisations. Reading textbooks is not recommended, particularly when these are found in public libraries and therefore very likely to be out of date. Even the most recent textbook will have been written a year or more before it reaches publication and parts will almost certainly be out of date. Clinicians supplement the information in textbooks by reading specialist medical journals and by attending conferences and meetings. A great deal of information can now be found on the Internet and especially on the World Wide Web. It is important to remember that anyone can place material on the Web and much of this is inaccurate and sometimes even dangerous. Leukaemia Research's website, www.lrf.org.uk, has links to many other sources of information on leukaemia and related diseases. Although we cannot guarantee the content of other websites we have selected those which seem likely to be the most reliable. It is usually best to start with a trustworthy organisation and follow links from that site rather than rely on typing a disease name into a search engine.

In seeking information it is important to always remember that the only person who can offer reliable advice is a doctor with the appropriate expertise and access to the patient's full notes. In particular it is important to be aware that each individual will respond differently to treatment and, even in those diseases which have less promising outlooks, many patients will do better than average.

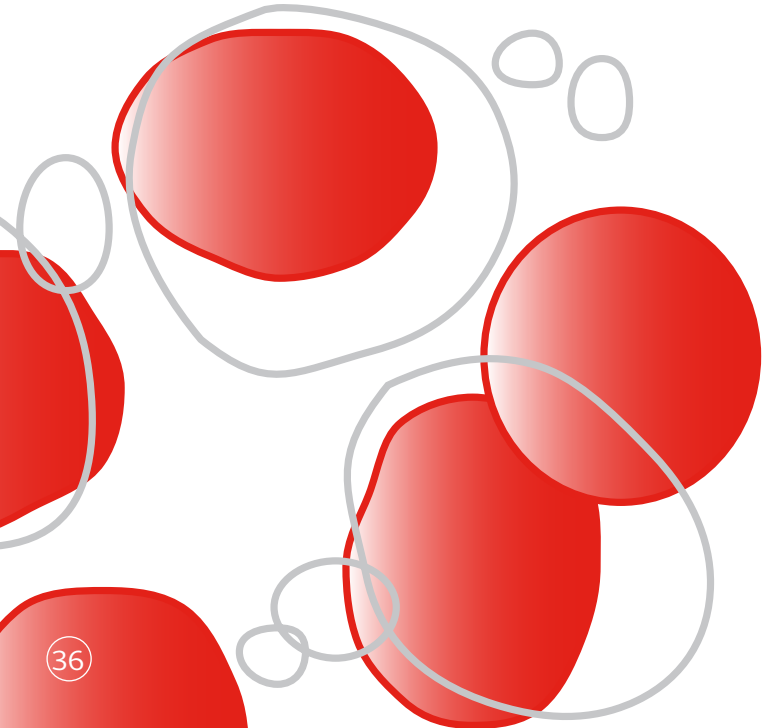


Useful contacts

Macmillan Cancer Support
Tel: 0800 808 2020
Fax: 020 7840 7841
Website: www.macmillan.org.uk

The Cancer Resource Centre
Tel: 020 7924 3924
Fax: 020 7978 6505
Website: www.cancer-resource-centre.org.uk

Leukaemia Care
Tel: 0800 169 6680
Website: www.leukaemiacare.org.uk



Dictionary of leukaemia and related diseases

The diseases

Acute leukaemia

A rapidly progressive cancer of the blood of sudden onset, characterised by the uncontrolled proliferation of immature blood cells which take over the bone marrow and usually spill into the blood stream. If left untreated it is fatal within a few weeks or months.

Acute lymphoblastic leukaemia (ALL)

A rapidly progressing cancer of the blood, affecting the type of white blood cell known as lymphocytes. Approximately 650 new cases are diagnosed every year in the UK. It is the most common form of childhood leukaemia.

Acute myeloid leukaemia (AML) or acute non-lymphocytic leukaemia

A rapidly progressing cancer of the blood affecting immature cells of the bone marrow, usually predominantly of the white cell population. Approximately 2,000 new cases are diagnosed each year in the UK. It is much more common in adults than in children.

Acute promyelocytic leukaemia (APL or APML)

This is one form of acute myeloid leukaemia. The condition responds particularly well to a drug called all trans retinoic acid which causes differentiation of the leukaemia cells which then die.

Amyloidosis

Amyloidosis is not a specific disease but the term for a group of conditions in which an abnormal substance called amyloid is deposited throughout the body. Amyloid is produced by plasma cells and amyloidosis may occur in association with multiple myeloma.

Aplastic anaemia

A rare disorder characterised by the failure of the bone marrow to produce blood cells. It may occur as an inherited condition (see Fanconi anaemia) or, more often, the disease develops later in life. This is called acquired aplastic anaemia. It leads to a severe shortage of all types of blood cell causing tiredness, susceptibility to infection and serious problems with bleeding.

Burkitt's lymphoma

A rapidly growing type of non-Hodgkin's lymphoma which usually affects the abdomen and requires immediate treatment. It responds well to specially designed chemotherapy.

Cancer

Diseases due to the uncontrolled growth and division of cells, often called malignant disease or neoplasia.

Chronic leukaemia

A cancer of the blood of gradual onset and generally of slow progression. It may be diagnosed by chance following a routine blood test and prior to the appearance of clinical symptoms.

Chronic lymphocytic leukaemia (CLL)

A slowly progressing form of leukaemia, characterised by an increased number of the type of white blood cells known as lymphocytes. With about 2,750 new cases occurring each year in the UK, it is the most common form of leukaemia in the UK and occurs predominantly in late middle age onwards. It has variable symptoms and course, but may be diagnosed by chance before the patient develops any clinical symptoms of disease.

Chronic myeloid leukaemia (CML) or chronic granulocytic leukaemia (CGL)

A leukaemia which is initially slowly progressing. There are approximately 750 new cases each year in the UK. It is characterised by the presence of large numbers of abnormal, mature granulocytes, circulating in the blood.

Chronic myelomonocytic leukaemia (CMML)

A form of myelodysplasia characterised by an increase in the number of circulating white blood cells of the monocyte type.

'Common' acute lymphoblastic leukaemia (cALL)

A subtype of acute lymphoblastic leukaemia affecting cells early in the B lymphocyte lineage which accounts for about 80% of all cases of acute lymphoblastic leukaemia.

Down's syndrome

A congenital condition in which some or all of the body cells have three copies of chromosome 21. This form of trisomy is associated with an increased risk of leukaemia.

Eosinophil leukaemia

Some patients with high eosinophil counts and abnormal bone marrow are classed as having eosinophil leukaemia. It may not always be obvious whether the diagnosis should be eosinophil leukaemia or hypereosinophilic syndrome. Some doctors consider eosinophil leukaemia to be a form of chronic myeloid leukaemia.

Erythroleukaemia

A rare cancer of the blood affecting immature red blood cells. This is a subtype of acute myeloid leukaemia, FAB M6.

Essential thrombocythaemia

A rare myeloproliferative disorder characterised by the production of large numbers of abnormal platelets. Symptoms include haemorrhage or thrombosis. Treatment varies according to the severity of the disease.

Extra nodal lymphoma

Literally 'outside the lymph nodes', but exhibiting the characteristics of lymph node cancer. A term used to describe the extent and site of disease.

Fanconi anaemia

A rare inherited type of aplastic anaemia which carries an increased risk to the patient of developing leukaemia. It may be treated by a bone marrow transplant.

Gammopathy

Normally the gamma globulins which make up antibodies are a mixture of a huge number of different types. When a gamma globulin is one particular form this is called monoclonal gammopathy. It arises from a clone of lymphocytes or plasma cells.

Hairy cell leukaemia

A rare leukaemia related to chronic lymphocytic leukaemia and characterised by the presence of abnormal cells with 'hairlike' projections. It occurs in middle age onwards. Therapy, if needed, is usually with chlorodeoxyadenosine.

Hodgkin's lymphoma

A type of lymphoma. There are approximately 1,400 new cases per year in the UK. Formerly known as Hodgkin's disease.

Hypereosinophilic syndrome

In some patients the number of eosinophils in the blood is markedly and persistently raised with no obvious cause such as a parasite infection. These patients have either hypereosinophilic syndrome (HES) or eosinophil leukaemia.

Idiopathic or autoimmune thrombocythaemia purpura (ITP)

A common disorder characterised by shortage of platelets with possible resultant bruising and spontaneous bleeding. Anti-platelet antibodies are detectable in some cases. It may present in either an acute (more common in children and following an infection) or a chronic form (more common in adults).

Monoclonal antibodies

Antibodies are made by cells belonging to a single clone. Current research is investigating their clinical application for targeted delivery of drugs to leukaemic cells and to purify cells used for bone marrow and stem cell transplants.

Large granular lymphocytic leukaemia (LGL)

A chronic leukaemia of T-cells that is usually associated with disease in other white cells and platelets or anaemia. LGL is a rare disease with important clinical differences from chronic lymphocytic leukaemia.

Leukaemia

From the Greek meaning ‘white blood’. Often referred to as cancer of the blood. Divided into many different types, some acute, others chronic. Characterised by the widespread uncontrolled proliferation of large numbers of abnormal blood cells, usually of the white cell lineages, which take over the bone marrow and often spill out into the blood stream. Other organs that may also be affected include lymph nodes, spleen, liver, testes, meninges, gums, and skin.

Li-Fraumeni syndrome

An inherited family trait carrying an increased risk of cancer during childhood and early adulthood.

Lymphoma

A cancer which originates in lymphoid tissue, including the lymph nodes (glands), liver, spleen, bowel, bone marrow, brain and occasionally other organs. The disease results from the uncontrolled production of lymphocytes. The general term includes over thirty different forms of the disease but there are two main categories: Hodgkin's lymphoma and non-Hodgkin's lymphoma.

Mast cell leukaemia

The mast cell is related to the monocyte/macrophage cells of the immune system and is found in most tissues. Excessive production of mast cells may be seen in the conditions systemic mastocytosis and mast cell leukaemia.

Monoclonal gammopathy of unknown significance

Different types of proteins called gamma globulin are produced to deal with different infections. Exclusive production of one form of gamma globulin is called monoclonal gammopathy. If there is no evidence of disease such as myeloma or lymphoma to explain the presence of a monoclonal gammopathy it is called monoclonal gammopathy of unknown significance (MGUS).

Monocytic leukaemia

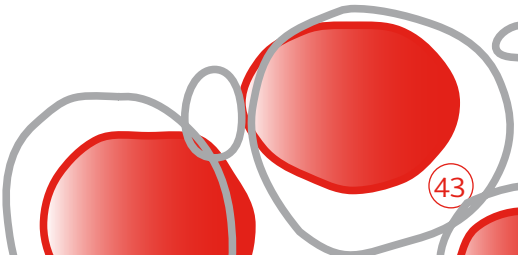
Cancer of the blood due to proliferation of cells of the monocyte series.

Multiple myeloma

A cancer caused by uncontrolled proliferation of the white blood cells called plasma cells within the bone marrow. The malignant cells do not usually accumulate in the blood and the tumour growth is restricted to the bones. This leads to bone destruction and is often associated with kidney problems.

Myelodysplasia or myelodysplastic syndromes (MDS)

A group of closely linked conditions in which the process of blood cell formation is disturbed by a failure of the immature cells to grow and develop normally. Sometimes referred to as ‘preleukaemia’, although only a minority of patients will ever develop leukaemia. Treatment may be based on supportive therapy or involve the use of chemotherapy.



Myelofibrosis or myelosclerosis

A disease in which the bone marrow is taken over by fibrous tissue and is no longer able to produce adequate numbers of mature blood cells. Often accompanied by enlargement of the spleen. It is occasionally found in cases of acute myeloid/lymphoid and chronic myeloid leukaemia. The primary form is classified as a myeloproliferative disorder.

Myeloproliferative disorders

A group of disorders characterised by the overproduction of blood cells by the bone marrow. One or more of the cell lineages may be involved and treatment varies according to the type and severity of the disease. See essential thrombocythaemia and polycythaemia rubra vera.

Non-Hodgkin's lymphoma

A group of lymphomas which differ in important ways from Hodgkin's lymphoma and are classified according to the microscopic appearance, cytogenetics and immunology of the cancer cells. The disease is classified as either indolent (slowly growing) or aggressive (rapidly growing) and may be treated in a variety of ways depending on the exact diagnosis.

Paroxysmal nocturnal haemoglobulinuria (PNH)

A rare disorder characterised by an increased rate of breakdown of red blood cells and decreased production of white blood cells and platelets. This leads to excretion of the red blood pigment, haemoglobin and its breakdown products, in the urine. There may be thrombosis of veins. The cause is unknown and the severity of disease variable. There is an association with aplastic anaemia.

Plasma cell leukaemia

The end stage of myeloma when immature plasma cells are found circulating in the blood.

Plasmacytoma

A localised area of myeloma-like disease, either in a bone or in the other tissues of the body. If there is only one such area it is called solitary plasmacytoma.

Polycythaemia rubra vera (PRV)

A condition characterised by the over-production of red blood cells by the bone marrow. Diagnosis is based on an increased number and volume of red cells. The total number of white blood cells and platelets may also be increased. The spleen is usually enlarged. Treatment will vary according to the age of the patient and severity of the disease. This condition carries a small risk of developing into acute leukaemia.

Pre-leukaemia

A general term referring to some bone marrow disorders, such as myelodysplasia which carry an increased risk of the patient developing acute leukaemia. The expression is misleading because only a minority of patients with these conditions develop leukaemia.

Prolymphocytic leukaemia (PLL)

A variant of chronic lymphocytic leukaemia in which the malignant cells have a more immature appearance. The disease requires chemotherapy and/or radiotherapy and sometimes removal of the spleen (splenectomy).

Refractory anaemia

A form of myelodysplasia which primarily affects red cell production by the bone marrow. In some cases the developing red cells show an internal ring of iron granules. These cells are called sideroblasts. Refractory anaemia (RA) and refractory anaemia with sideroblasts (RAS) are the most common forms of myelodysplasia.

Refractory anaemia with excess blasts (RAEB)

A form of myelodysplasia characterised by the build up of immature white blood cells (blasts) in the bone marrow. If the immature cells are particularly numerous it may indicate a chance of transformation to acute leukaemia and the condition is called RAEB in transformation (RAEBt).

Richter's syndrome

Development of an aggressive, often localised, lymphoma in a patient who has chronic lymphocytic leukaemia.

Secondary leukaemia

A leukaemia arising from either previous chemotherapy or radiotherapy or as the development of a pre-existing condition, such as myelodysplasia or polycythaemia rubra vera.

Waldenstrom's macroglobulinaemia

A rare disorder which has features in common with an indolent non-Hodgkin's lymphoma and with multiple myeloma. The progression of the condition more closely resembles indolent non-Hodgkin's lymphoma.

Drugs used in treatment

Alkylating agents

Anti-leukaemic drugs which interact with genetic material (DNA) in such a way as to prevent division of the cells. Drugs of this type include busulphan, chlorambucil, cyclophosphamide, melphalan.

Allopurinol

This is a drug which prevents build-up of uric acid (produced by breakdown of proteins when cells are killed). Large quantities of uric acid in the blood lead to crystal deposits in joints this is the cause of gout or can lead to kidney damage.

Anthracyclines

Drugs which are used in leukaemia therapy to prevent cell division by disrupting the structure of the DNA. Drugs of this type include buridazone, daunorubicin, doxorubicin (Adriamycin), epirubicin, and idarubicin.

Antibiotics

Drugs which kill or stop the growth of bacteria, for example penicillin.

Anti-emetic

A drug to prevent or alleviate the nausea and vomiting which sometimes occur as side-effects of chemotherapy. Drugs of this type include metoclopramide (Maxolon), ondansetron, Zofran.

Antilymphocyte globulin

Antibodies which attach to and destroy lymphocytes. They may be used clinically by injection into a vein, for example in aplastic anaemia. One form, called antithymocyte globulin, acts specifically against T cells.

Antimetabolites

A group of anti-cancer drugs which prevent cells growing and dividing by blocking the chemical reactions required in the cell to produce DNA. Drugs of this type include 6-mercaptopurine, azathioprine, thioguanine, methotrexate.

Bisphosphonate

A group of drugs used in multiple myeloma which do not affect the disease directly but reduce the bone damage and associated pain.

Chemotherapy

Treatment using anti-cancer drugs. These may be used singly or in combination to kill or prevent the growth and division of cells. Although aimed at the cancer cells, chemotherapy will also unavoidably affect rapidly dividing normal cells such as in the hair and gut causing hair loss and nausea, which are usually temporary and reversible.

Corticosteroids (steroids)

A group of synthetic hormones including prednisone, prednisolone, methylprednisolone and dexamethasone used in the treatment of some leukaemias and myeloma. Also used to suppress graft rejection and graft versus host disease following a stem cell transplant. Side-effects include an increased risk of infection, rise in blood pressure, peptic ulcers, diabetes mellitus, osteoporosis.

Cyclosporin A

A drug used to prevent and treat rejection and graft versus host disease in transplant patients by suppressing their normal immune system.

Cytotoxic drugs

Anti-cancer drugs which act by killing or preventing the division of cells.

Diuretic

A drug to stimulate the excretion of urine by the kidneys. May be used during chemotherapy to ensure the excretion of anti-cancer drugs.

Folic acid antagonist

A chemical which inhibits a cell's capacity to use folic acid and so prevent cell division, for example methotrexate.

Gamma globulin

A concentrated solution of antibody given through a vein to fight infections, e.g. measles in patients with low resistance.

Glivec

Brand name for imatinib mesylate. This is a drug which specifically blocks the effect of BCR-ABL — an abnormal gene found in CML and other malignancies.

Interferons

A family of proteins derived from human cells that are involved in fighting viral infections. They are now available as products of genetic engineering for use in the treatment of a number of leukaemias and leukaemia related diseases including hairy cell leukaemia, and multiple myeloma.

Thalidomide

A drug which is being used for treatment of myeloma. Causes foetal abnormalities if taken during pregnancy. New drugs based on thalidomide are being developed.

Velcade

Brand name for bortezomib — a drug which is showing promise in treatment of myeloma and some types of lymphoma.

Vinca alkaloids

Anti-cancer drugs originally derived from vinca (periwinkle) plants. Drugs of this type include vincristine and vinblastine.

Zig (zoster immune globulin)

Gamma globulin against the chicken pox virus which can be given to an immunosuppressed patient following direct contact with the disease to prevent infection.

General terminology

Aetiology

The scientific study of the factors which cause a disease, e.g. environmental factors such as infections and radiation.

Allogeneic stem cell transplant

Also called an allograft. A transplant using stem cells collected from a 'matched' healthy donor, usually a brother or sister. The risks associated with the transplant increase with age.

Alopecia

The loss of hair. A side-effect of some forms of chemotherapy or radiotherapy used to treat leukaemia and other cancers. Usually temporary.

Anaemia

Deficiency in the oxygen-carrying pigment haemoglobin in the blood. Causes pallor, tiredness and breathlessness.

Anorexia

Loss of appetite.

Antibodies

Naturally produced substances in the blood which destroy or neutralise specific toxins or 'foreign bodies', for example viruses. They are produced by white blood cells known as lymphocytes in response to exposure to antigens.

Antigen

A substance which stimulates cells of the body's defence system to react against it by producing antibodies.

Aplasia

Failure of production of blood cells in the bone marrow because of a lack of stem cells. Usually this condition affects all types of blood cells and is called aplastic anaemia.

Auto-immune disease

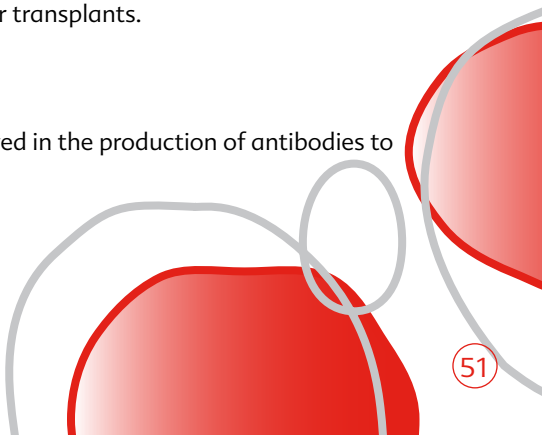
Diseases caused by an individual's immune system producing antibodies against tissues of its own body.

Autologous stem cell transplant (ASCT)

A blood stem cell transplant using the patient's own marrow or peripheral blood stem cells which have been collected and stored at an early-stage of the disease, also called autograft. The marrow may be manipulated in the laboratory, a procedure called purging, to try to ensure there is no contamination with leukaemia cells. This type of procedure may be carried out in even older patients in contrast to donor transplants.

B lymphocyte (B cell)

A type of white blood cell normally involved in the production of antibodies to combat infection.



Bacteria

Microscopic organisms which cause many types of infectious disease, for example pneumonia. Patients have a reduced ability to fight infections following chemotherapy or bone marrow transplantation. This may mean that even harmless bacteria, for example those which are normally found on the skin, may cause serious illness.

Basophil

A type of white blood cell which is involved in allergic and inflammatory reactions. Normally present in low numbers in the blood.

Basophilia

An increase in the number of basophils in the blood.

Bence-Jones protein

A characteristic protein found in the urine of some patients with multiple myeloma. It is derived from the antibodies produced by the cancerous myeloma cells and can be used to help in diagnosis of the disease and to monitor the effects of treatment.

Benign

Non-cancerous growths that may or may not need to be surgically removed.

Biopsy

A small sample of fresh tissue, for example lymph node or bone marrow, removed for laboratory analysis to establish or confirm an exact diagnosis of disease.

Blast cells

Immature blood-forming cells which normally represent up to 5% of the cells in the bone marrow. They are not present in healthy blood. Acute leukaemia is characterised by over-production of abnormal blast cells which take over the bone marrow and often spill out into the blood stream.

Blast crisis

Aggressive phase of chronic myeloid leukaemia or polycythaemia rubra vera characterised by the production of large numbers of immature cells which may be either of the myeloid or lymphoid type. Clinically similar to acute leukaemia and more difficult to treat than chronic phase disease.

Blood cells

There are three main types of cells in the blood stream; the red cell, which carries oxygen, the white cell, which fights infections, and the platelets, which help prevent bleeding. The correct balance between each cell type must be maintained. Production of blood cells is controlled by natural chemicals called growth factors which may be used in treatment.

Blood count

A routine test requiring a small blood sample to estimate the number and types of cells circulating in the blood.

Bone marrow

The tissue which produces the blood cells. It is found within the hollow cavities of many of the bones of the body. Bone marrow contains the stem cells from which all blood cells are derived. Examination of the bone marrow is an important part of the diagnosis of leukaemia and the monitoring of treatment.

Bone marrow aspirate

A small volume of bone marrow removed under local or general anaesthetic from either the hip bone (pelvis) or breast bone (sternum). The cells in the sample can then be examined under the microscope to identify any abnormality in the developing blood cells. A trephine biopsy, where a small 'core' of bone marrow is removed under local anaesthetic may be taken at the same time.

Bone marrow transplant (BMT)

A procedure used in the treatment of a variety of blood disorders including leukaemia, lymphoma and sometimes myeloma. The patient receives very high doses of chemotherapy and/or radiotherapy to treat the disease and produce immunosuppression. This damages the bone marrow and makes the blood count fall. Replacement marrow is taken from a matched donor (allogeneic bone marrow transplant) or from the patient themselves (autologous bone marrow transplant) under a general anaesthetic and returned to the patient through a vein (or central venous line) in a similar way to a blood transfusion. Peripheral blood stem cells may be used instead, especially for autografts.

Candida

A type of fungus, Candida infection in the mouth (oral thrush) is a common problem for immunosuppressed patients.

Cannula

A tube for insertion into the body, usually into a vein, via a sharp needle type fitting which is then withdrawn from the cannula to allow fluids to pass through the tube.

Carcinogenesis

The development of cancer.

Carcinogen

A substance which has the ability to cause cells to become cancerous.

CAT scan (CT scan)

Computer assisted tomography (CAT) is a sophisticated X-ray technique used to produce detailed internal images of the body, particularly the chest and abdomen. The patient lies on a couch which gradually moves through the X-ray machine and the image is built up by a computer as a cross section through the body.

Catheter

A hollow tube inserted into organs of the body for admitting or removing gases or liquids. For example, for the removal of urine from the bladder.

Cell biology

The study of the structure, composition and function of cells.

Cell markers

Biochemical or immunological characteristics which distinguish and discriminate between different cell types. HLA-antigens are one type of cell marker.

Cells

The individual units from which tissues of the body are formed.

Central nervous system (CNS)

The brain and spinal cord.

Central venous line

A catheter passed through a blood vessel into a large central vein, used for patients undergoing intensive therapy and to provide a route for taking blood samples and administering drugs without repeated needle puncture of a vein. There are various types including indwelling catheters and implanted reservoirs. If you require a central venous line a doctor or nurse will discuss this with you.

Cerebrospinal fluid (CSF)

This fluid surrounds and protects the brain and spinal cord. Samples can be obtained by lumbar puncture.

Chromosomes

Chromosomes carry the 30,000 or so genes which provide the inherited blueprint of each individual. In humans there are normally 23 pairs contained in the nucleus of each cell. Alterations in the number or organisation of the chromosomes may play a key role in the development of cancer.

Clinical trial

A carefully monitored assessment of new forms of treatment. They can vary in design and size from trials of innovative treatments involving small numbers of patients to large national trials which compare variations in current therapies. A patient will always be informed when their treatment is part of a trial.

Clone

A population of genetically identical cells arising from a single parent cell. Leukaemia cells originate from one original abnormal cell producing a 'leukaemic clone'.

Clotting factors

A group of chemical constituents of the blood (factors I to XIII) which interact to make the blood clot.

CNS leukaemia

Invasion of the brain or spinal cord by leukaemic cells. This may be diagnosed by examination of the surrounding cerebrospinal fluid.

Coagulation

Clotting of the blood. A complex reaction depending on a series of biochemical components (clotting factors) and platelets in the blood.

Congenital

A term used to describe deformities or diseases which are present at the time of birth.

Consolidation treatment

A course of treatment with anticancer drugs given to the patient whilst in remission with the aim of killing any remaining cancerous cells.

Cord blood

Blood obtained from the umbilical cord at the time of birth and which derives from the baby.

Cord blood stem cells

Stem cells recovered from cord blood which have been shown to have the capability to repopulate bone marrow and produce blood cells.

Cytogenetics

The study of the structure of chromosomes. Cytogenetic tests are carried out on samples of blood and bone marrow taken from leukaemia patients to detect any chromosomal abnormalities associated with the disease. These help in the diagnosis and selection of optimal treatment.

Cytomegalovirus

A virus which is harmless in healthy people but may cause serious disease in severely immunosuppressed patients. Particularly dangerous following a bone marrow transplant.

Cytopenia

A reduction in the number of cells circulating in the blood.

Deletion

A chromosome abnormality in which part of a single chromosome has been lost.

Depletion

A laboratory procedure for reducing the numbers of specific cell types within bone marrow donated for transplantation, for example the removal of some types of lymphocytes. This may be to avoid 'mismatch' problems (particularly in relation to unrelated donor transplants) or to remove a sub-set of potentially leukaemic cells in an autograft.

Differentiation

The gradual maturation of a cell whereby its functions and properties become increasingly specialised. Leukaemic cells are often poorly differentiated, i.e. they show immature characteristics.

Disseminated disease

Disease in which the cancerous cells have spread from the tissue of origin to other organs.

DNA

Deoxyribonucleic acid (DNA) provides the essential building block for storing genetic material. There are four different chemical components of DNA (bases) arranged in coded sequence as genes which determine an individual's inherited characteristics.

Donor lymphocyte infusion

If a patient who has had an allogeneic bone marrow transplant has a relapse, with return of the original disease, they may be given lymphocytes from the donor. This may eliminate the leukaemia cells.

Eosinophil

A type of white blood cell involved in inflammatory, allergic or antiparasitic responses. Usually present in the circulation in very low numbers.

Eosinophilia

Increased numbers of eosinophils in the blood. It occurs in some cases of Hodgkin's lymphoma, in asthma, hay fever and parasitic infections, hypereosinophilic syndrome and eosinophil leukaemia.

Epidemiology

The science of studying the occurrence of disease in populations and relating this to genetic and/or environmental causes.

Epstein-Barr virus

A common virus which causes glandular fever. Also associated with Burkitt's lymphoma. There is some evidence of a link between Epstein-Barr virus infection and Hodgkin's lymphoma.

Folic acid

A form of vitamin B obtained from green leafy vegetables, e.g. spinach. It is essential for synthesis of DNA and therefore the growth and division of cells.

Fungus

An infective agent such as a mould or yeast, causing particular problems in immunosuppressed patients, for example Candida.

Genes

Formed from DNA and carried on the chromosomes, genes direct the activities of cells. They are responsible for the synthesis of proteins and so the inherited characteristics which distinguish one individual from another. Each human individual has an estimated 30,000 separate genes.

Graft rejection

Rarely, when a patient has an allogeneic bone marrow transplant, the new bone marrow will fail to start producing blood cells. This is called graft rejection. It may be possible to do a second transplant.

Graft versus host disease (GvHD)

A common, and serious, complication of bone marrow transplantation. Some of the donor's immune cells reject the patient's own cells as foreign. The skin, liver and gut may be affected. It can occur in either chronic or acute forms and is treatable by immunosuppressive drugs.

Graft versus leukaemia (GvL)

The effect of allografted stem cells in attacking leukaemia cells in the recipient. If graft versus host disease is present but not severe, it may be beneficial in helping to kill off leukaemia cells. If all the T-lymphocytes are removed from an allogeneic bone marrow transplant it minimises the risk of graft versus host disease but increases the risk of relapse.

Granulocyte

A type of white blood cell. They protect the body against infection by seeking out and killing microorganisms.

Growth factors

A complex family of proteins produced by the body to control growth, division and maturation of blood cells by the bone marrow. Some are available as products of genetic engineering, and are used clinically to stimulate normal white cell production following chemotherapy or bone marrow transplantation, for example G-CSF, GM-CSF.

Growth hormone

A biochemical secreted by a gland in the brain which controls growth and is of particular importance during adolescence. Radiotherapy given to the head and neck of children with leukaemia may lead to a deficiency in growth hormone. This may be replaced by intravenous injection.

Haematologist

A doctor specialising in the diagnosis and treatment of blood diseases.

Haematology

The study of blood diseases including leukaemia.

Haemopoiesis or haematopoiesis

Term to describe the production and maturation of blood cells from very primitive stem cells. This takes place in the bone marrow which is a spongy tissue in the middle of bones.

Haemoglobin

The iron containing pigment in red blood cells which carries oxygen around the body. Lack of haemoglobin is called anaemia . Normal values are 13.5 to 17.5 g/100ml of blood in males, 11.5 to 15.5 g/100ml in females.

Haemorrhage

Bleeding either to the outside through the skin or internally.

Hepatitis

Inflammation of the liver.

Hepatomegaly

Enlargement of the liver.

Histology

The investigation of tissue samples by chemical and microscopical analysis.

HLA-Antigens

A complex family of genetically inherited proteins which are found on the surface of cells throughout the body. They determine the 'match' between patient and potential donor in bone marrow transplantation. HLA factors are inherited from the mother and father and so the greatest chance of having the same HLA-type is between brothers and sisters, that is 1 in 4.

HTLV

Human T cell lymphotropic virus. A family of viruses which invade T cells. This includes a rare leukaemia virus, HTLV-1, found primarily in Japan and the Caribbean, causing an increased incidence of T cell leukaemias in these populations.

Hypercalcaemia

Increased levels of calcium in the blood. It is often associated with multiple myeloma due to degradation of the bones. It is dangerous if not controlled.

Iatrogenic disease

A disease produced as a consequence of medical or surgical treatment.

Idiopathic

Term applied to diseases to indicate that their cause is unknown.

Immune deficiency

Impaired ability of the body's defence mechanisms to combat infections by bacteria, viruses and fungi.

Immune response

The reaction of the body to an antigen, for example an infectious agent, or to the tissues of another individual as in the rejection of an organ transplant.

Immunoglobulins

Proteins in the blood plasma which function as antibodies and play an important part in controlling infections.

Immunosuppression

A treatment induced reduction in the body's defence mechanisms. Deliberate immunosuppression is a necessary part of the bone marrow transplant procedure to prevent graft versus host disease and graft rejection.

Intensification

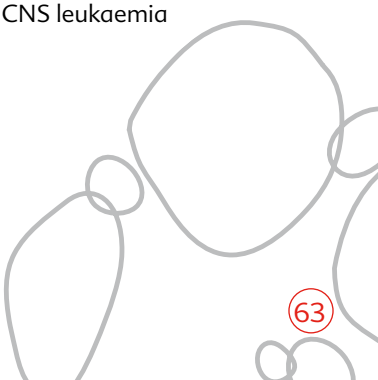
Increasing the amount, number or combination of anti-cancer drugs given to a patient in an attempt to kill drug-resistant or residual leukaemic cells.

Intramuscular injection

Injection into the muscle.

Intrathecal injection

Injection of drugs into the spinal fluid to prevent or treat CNS leukaemia or lymphoma.



Intravenous infusion

Administration of antibiotics, blood products, anti-cancer drugs or nutrients into a patient's vein over a prolonged period of time.

Intravenous injection

The application of drugs into a vein through a syringe.

In vitro

Literally meaning 'in glass'. Used to describe studies carried out on living cells or tissues grown in the laboratory.

In vivo

Used to describe studies in living tissue or in a whole organism.

Karyotype

Analysis to check the number, form and structure of chromosomes.
This can give valuable information to aid in the diagnosis and the selection of treatment.

Karyotypic abnormality

Abnormality in the number, form or structure of chromosomes. Particular abnormalities are associated with particular subtypes of leukaemia.

Late-effects

Results of chemotherapy and/or radiotherapy which only become apparent with long-term monitoring of the patient over a period of years. These are of particular concern in patients below the age of puberty.

Leukaemogenesis

The development of leukaemia.

Leukapheresis

Method of separating blood into its liquid and cellular components and for the removal of white blood cells before returning the remainder of the blood to the patient. It is used to reduce the white cell count when chemotherapy is to be avoided, for example during pregnancy.

Leukocytes

Collective term for white blood cells.

Leukopaenia

Condition in which the number of white cells in the blood is greatly reduced. Leads to increased risk of infections.

Lineage

Describes cells with a common ancestry, that is developing from the same type of identifiable immature cell.

Long-term survival

Term used to describe the survival of leukaemia patients who have been disease free for prolonged periods of time, usually at least five years. The chance of disease returning (relapse) decreases with time.

Lumbar puncture

A procedure for removing spinal fluid from around the spinal cord using a fine needle in the lower part of the back. Samples are analysed for evidence of any CNS leukaemia. Also used to administer anti-cancer drugs to either prevent or cure CNS disease.

Lymph nodes or glands

Small structures found throughout the body, e.g. neck, groin, armpits, abdomen, which contain both mature and immature lymphocytes.

Lymphatic system

This consists of the spleen, lymph nodes, lymphatic vessels and areas of lymphoid tissue such as the tonsils. It plays a major part of the body's immune response.

Lymphocyte

A type of white blood cell which is involved in the immune defences of the body. There are two main types B cells and T cells.

Lymphoid

Referring to the lymphatic system including lymphocytes and lymph nodes.

Lymphoproliferation

An increase in the production of lymphocytes. This may occur as a normal response to infection.

Macroglobulinaemia

In certain conditions, such as Waldenstrom's macroglobulinaemia, affected lymphocytes produce an excess amount of an abnormal antibody known as IgM. This is called macroglobulinaemia.

Macrophage

A type of white blood cell which migrates from the blood into tissues and acts as a scavenger, ingesting particles such as bacteria.

Magnetic resonance imaging

A body scanning technique which uses an intense magnetic field to generate images of the internal organs. Properties of normal and cancerous tissue differ, allowing malignant tumours to be visualised by computer processing of the signals detected.

Maintenance treatment

Treatment given for a period of months or years to maintain remission and eliminate any residual leukaemic cells in the body, usually for acute lymphoblastic leukaemia.

Malignancy

A term applied to tumours characterised by the uncontrolled proliferation of cells. See also cancer.

Megakaryocyte

Large cell in the bone marrow which produces platelets.

Monoclonal

Proteins made by cells which all belong to the same clone are identical and are called monoclonal.

Monocyte

A type of white blood cell of relatively large size which acts as a scavenger and ingests large particles.

Monosomy

Term which indicates the loss of a whole chromosome.

MRC (Medical Research Council)

Government funded body 'to promote the balanced development of medical and related biological research' in the UK. It organises national clinical trials for the assessment of new treatment protocols for leukaemia and some of the related diseases.

Mucositis

Inflammation of the lining of the mouth and throat which may be caused by anti-leukaemia drugs.

Multi-drug resistance (MDR)

Multi-drug resistance occurs when leukaemia cells eliminate anti-cancer drugs before a high enough concentration to kill the cells is achieved. Resistance against most drugs will make the leukaemia very difficult to treat.

Mutation

A minute genetic change to DNA caused, for example, by exposure to hazardous chemicals or copying errors during cell division. If these affect normal cell function they can lead to disease development.

Myeloblasts

Immature cells of the myeloid series.

Myeloid

Collective term for the non-lymphocyte groups of white blood cells. It includes cells from the granulocyte, monocyte, red cell and platelet lineages.

Myelomonocytic

A condition which affects both the myeloid and monocytic cells.

Myelopoiesis

The process of production and maturation of myeloid cells.

Neuropathy

Damage to the nerves which may occur as a complication of antileukaemia treatment. It usually affects the peripheral nerves (nerves to the arms and legs) and may be reversible when treatment is stopped or reduced.

Neutropaenia

A condition in which the neutrophil count is reduced. It may be caused by high dose chemotherapy and carries an increased risk of infection.

Neutrophil

The most common type of cell within the granulocyte group of white blood cells.

Oncogenes

Genes carrying the potential to cause cancer.

Oncologist

A specialist in the diagnosis and treatment of cancer.

Packed cell volume or haematocrit

Measurement of the proportion of the blood occupied by the red blood cells. Normal values are 40-54% in males, 35-47% in females.

Palliative care

Treatment aimed at relieving symptoms and pain rather than effecting a cure.

Pancytopaenia

Condition in which there are reduced numbers of all types of blood cells.

Paraprotein

Paraprotein is a form of antibody characteristic of, and produced by, a clone of cells of the B cell type, for example in multiple myeloma. Its presence in the blood acts as an important marker of disease.

Pathogenesis

Development of a disease.

Pathologist

A doctor who specialises in the cause and diagnosis of disease and how disease affects the organs of a body.

Peripheral blood stem cell (PBSC)

There are small numbers of stem cells in the circulation. These are known as peripheral blood stem cells.

Peripheral blood stem cell transplant

The use of peripheral blood stem cells as an alternative to bone marrow transplantation. The stem cells are obtained by using growth factors given to the donor to increase numbers in the circulation to a level where they can be harvested.

Petechiae

Small red or purple pin-head spots on the skin. They are small haemorrhages and usually the result of a shortage of platelets.

Pharmacokinetics

The study of the action of a drug in the body over a period of time, including the processes of absorption, metabolism and excretion.

Phenotype

The characteristic appearance and function of a cell or tissue.

Philadelphia chromosome

An abnormal chromosome associated with chronic myeloid leukaemia and some cases of acute lymphoblastic leukaemia. The Philadelphia chromosome is formed when part of chromosome 9 attaches to chromosome 22. This abnormality is found in nearly all cases of chronic myeloid leukaemia.

Plasma cells

Large cells derived from lymphocytes that form antibodies. These are not normally found in circulating blood but restricted to bone marrow and lymph nodes.

Plateau phase

Stable stage of disease in multiple myeloma following good response to anti-cancer treatment.

Platelets or thrombocytes

They are tiny cell-like bodies derived from Megakaryocytes in the bone marrow. Platelets circulate in the blood and play an important role in the prevention and control of bleeding. Normal values, 150-400 x 10^9 per litre.

Prolymphocyte

An early lymphocyte precursor. Not commonly seen in the blood but in prolymphocytic leukaemia they may be present in large numbers.

Prophylaxis

Precautionary treatment given with the aim of preventing a disease occurring.

Progenitor cell or precursor cell

Immature cell in the bone marrow which is responsible for producing mature blood cells.

Prognosis

An assessment of the likely course of disease for a patient, particularly concerning the chances of cure and complete recovery or length of survival.

Protocol

A schedule of treatment. For example, the number, frequency and timing of administration of a course of anti-cancer drugs.

Pruritis

Itching, sometimes severe, which may be a significant problem in lymphoma.

Purging

The laboratory treatment of bone marrow harvested for an autologous bone marrow transplant or peripheral blood stem cell transplant to remove any residual leukaemic cells in order to reduce the chance of relapse. The use of this procedure varies between treatment centres and depends on the type of leukaemia being treated.

Purpura

A condition characterised by the occurrence of purple spots on the skin, often accompanied by bleeding from the gums.

Radiology

The use of X-rays in the diagnosis of a disease.

Recombinant

A term used to describe drugs which have been produced using the techniques of genetic engineering. The products are exact equivalents of compounds produced naturally by the body.

Red blood cells or erythrocytes

The cells of the blood which contain the red pigment haemoglobin and carry oxygen to all the tissues of the body. Normal red cell count in the blood is $4.5\text{-}5.0 \times 10^{12}$ per litre.

Radiotherapy

The use of X-rays and other forms of radiation in treatment. Radiotherapy kills cancer cells in the area of the body being treated and is therefore effective treatment for localised disease, particularly in lymphoma and multiple myeloma. Side-effects vary according to the type of treatment and will be discussed with the patient by the hospital staff.

Reed-Sternberg cell

A distinctive abnormal cell seen in Hodgkin's lymphoma.

Relapse

The recurrence of disease. In leukaemia this may be indicated by changes in the blood, bone marrow, CNS or testes even before the patient experiences any symptoms.

Remission

Restoration of the blood, bone marrow and general health of the patient to normal, induced by chemotherapy and/or radiotherapy.

Remission induction or induction treatment

The initial course of treatment given to patients on admission to hospital to remove all clinically detectable cancer.

Reticulocytes

Immature red blood cells normally present in the blood stream in very low numbers (0.2-2%). Raised numbers of reticulocytes may be found as a result of increased red cell production in the bone marrow, for example following haemorrhage.

Retinoic acid

A synthetic compound related to vitamin A which can stimulate cells to become fully mature. It may be used clinically to treat some forms of leukaemia, notably a subtype of acute myeloid leukaemia called acute promyelocytic leukaemia.

Retrovirus

A class of virus including the HTLV-1 retrovirus that causes a rare form of human leukaemia.

RNA (Ribonucleic acid)

A copy of the genetic code used by cells as a template for making proteins.

Septicaemia

This is a general term to describe serious bacterial infection of the blood stream often associated with high fever.

Serum

The part of the blood which remains after cells, platelets and fibrinogen have been removed.

Sibling

Brother or sister.

Spleen

The spleen acts as a 'discriminating filter' of the blood. It can selectively remove old red blood cells and bacteria and other foreign bodies. The spleen also acts as a store for platelets. It is often enlarged in leukaemia.

Splenectomy

Surgical removal of the spleen. This is sometimes done in leukaemia or lymphoma as part of a patient's treatment.

Splenomegaly

Enlargement of the spleen.

Staging

An assessment of the spread of disease through the body, for example in lymphoma. It is of importance for the selection of optimal treatment.

Stem cells

The most primitive cells in the bone marrow from which all the various types of blood cell are derived.

Subcutaneous injection

An injection into tissue immediately under the skin.

Syngeneic

Literally 'sharing the same genes'. It refers to bone marrow or peripheral blood stem cell transplants between identical twins.

T lymphocyte

A type of white blood cell derived from the thymus (hence T cells) involved in controlling immune reactions and in fighting viral infections. Uncontrolled proliferation of this type of cell gives rise to T cell leukaemia/lymphoma.

Testicular relapse

Recurrence of leukaemia in the testicles. The disease may be restricted to the testicles or may also be present in either the bone marrow or CNS. Treatment will depend on the timing and extent of relapsed disease.

Thrombocythaemia

An over-production of platelets.

Thrombocytopaenia

Shortage of platelets, leading to problems with bleeding.

Thrombosis

The development of a clot in a blood vessel, usually in a vein but sometimes in an artery. It is potentially life-threatening if left untreated.

Thymus

A gland at the base of the neck concerned with the production of functional T cells.

Tomography

An X-ray picture of internal organs of the body.

Total body irradiation (TBI)

Radiotherapy often given in several doses prior to bone marrow transplantation with the aim of killing any residual leukaemia in the patient. It is used in conjunction with high dose anti-cancer drugs. The procedure and its side-effects will be discussed individually with the patient.

Transformation

A term to describe either the change of a normal cell into a cancerous cell, or the acceleration of chronic myeloid leukaemia to a more acute phase characterised by the production of large numbers of blast cells.

Translocation

A chromosome abnormality in which the part of one chromosome has become transferred to another. See also Philadelphia chromosome.

Trephine biopsy

Removal of a small ‘core’ of bone marrow under local anaesthetic. It is used to assess bone marrow structure, the number and distribution of all the blood cell types. The trephine biopsy is normally done at the same time as a bone marrow aspirate.

Virology

The study of viruses and viral diseases.

Virus

A minute infective agent which depends on the cell it infects for its replication and survival.

Trisomy

Term which indicates the presence of an additional whole chromosome.

Tumour

An accumulation of abnormal cells which may be benign or malignant.

Ultrasonography (ultrasound)

Pictures of the body's internal organs built up from the interpretation of reflected sound waves.

White blood cells (leukocytes)

They comprise several different types of cells within three main types: granulocytes (mainly consisting of neutrophils), lymphocytes and monocytes. They are formed in the bone marrow and it is their uncontrolled proliferation which leads to leukaemia. Normal values are within the range 4.5-11.0 x 10^9 per litre.

X-rays

Used in diagnosis and staging of lymphoma and multiple myeloma. Also used to diagnose, for example, a chest infection.

Notes

Notes

Typical normal values for blood test results

	WBC x 10^9/l	RBC x 10^{12}/l	Hb g/dl	ANC x 10^9/l	Platelets x 10^9/l
Adult male	3.7 to 9.5	4.3 to 5.7	13.3 to 16.7	1.7 to 6.1	143 to 332
Adult female	3.9 to 11.1	3.9 to 5.0	11.8 to 14.8	1.7 to 6.1	143 to 332
West Indian	2.8 to 9.8			1.0 to 6.5	122 to 374
African	2.8 to 7.8			0.9 to 4.2	115 to 342
Child 2-5 yrs	5 to 13	4.2 to 5.0	11 to 14	1.5 to 8.5	143 to 332
Child 6-9 yrs	4 to 10	4.3 to 5.1	11 to 14	1.5 to 6.0	143 to 332
Child 9-12 yrs	4 to 10	4.3 to 5.1	11.5 to 15.5	1.5 to 6.0	143 to 332
Normal ranges vary slightly between laboratories so you may wish to ask your doctor to enter your normal values below:					

WBC	White blood cell count
RBC	Red blood cell count
Hb	Haemoglobin concentration
ANC	Absolute neutrophil count

Separate ranges are quoted for West Indian and African populations as these groups have different normal ranges for white cell counts, absolute neutrophil counts and platelet counts.

This information is adapted, with permission, from *A Beginner's Guide to Blood Cells*, Dr Barbara Bain. Pub. Blackwell, Oxford, 1996.

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Leaflets on a range of associated blood disorders are also available

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