

Acute Myeloid Leukaemia (AML)

Acute myeloid leukaemia is a cancer of blood forming cells in the bone marrow. Abnormal immature white blood cells (blasts) fill the bone marrow and spill into the bloodstream. Production of normal blood cells is affected causing anaemia, bleeding problems, and infections. Treatment is mainly with chemotherapy. The outlook varies and depends on such things as the exact sub-type of the AML, and your age.

What is leukaemia?

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

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

What is normal blood made up of?

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

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

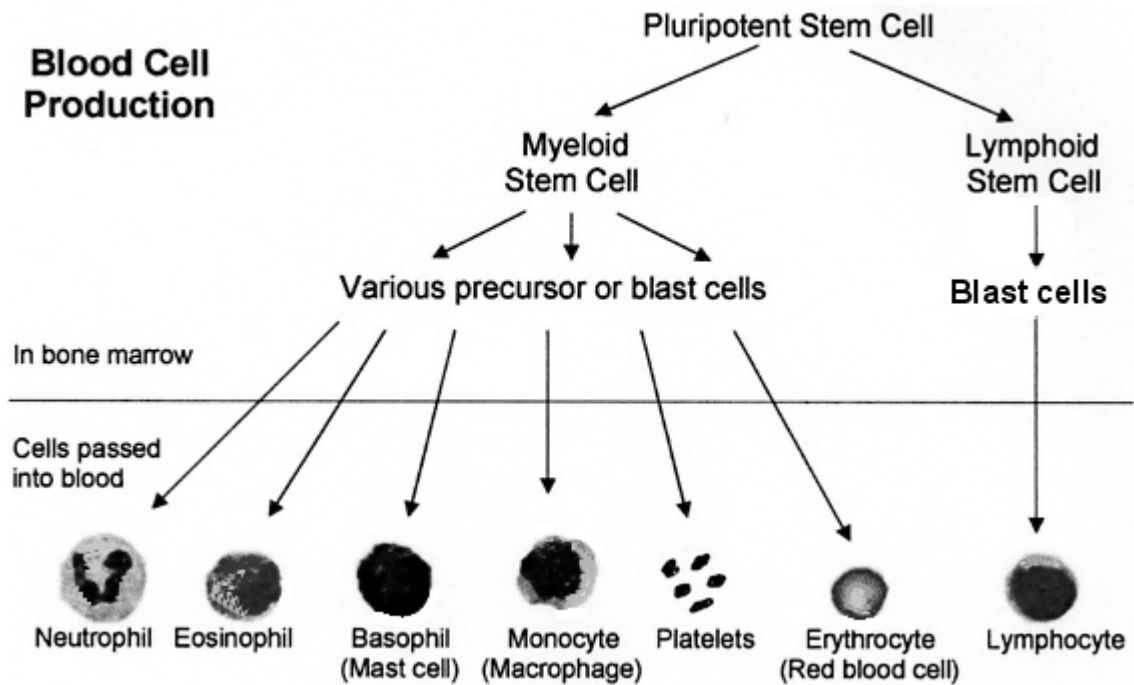
The bone marrow, stem cells and blood cell production

Bone marrow

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

Stem cells

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



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

Blood production

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

The main types of leukaemia are:

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

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

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

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

What is acute myeloid leukaemia?

Acute myeloid leukaemia (AML) is a condition where the bone marrow makes large numbers of abnormal immature white blood cells which are derived from a myeloid stem cell. The abnormal immature cells are called blasts.

There are various sub-types of AML, depending on exactly what cell type becomes cancerous and at what stage in the maturing process. There are eight main subtypes which are called M0, M1, M2...etc to M7. These are sometimes called more descriptive names such as 'Acute myelomonocytic leukaemia' (this is M4 where the blast cell is one which would normally have developed in to a monocyte), and 'Acute myeloid leukaemia with minimal evidence of myeloid differentiation' (this is M0 where the blast cell is a very immature cell), etc.

Typically, AML develops quite quickly (acutely) and rapidly becomes worse (over a few weeks or so) unless treated.

Who gets acute myeloid leukaemia?

AML is an uncommon disease and affects about 2000 people in the UK each year. Most cases occur in people aged over 40. AML is rare in people under the age of 20. It is slightly more common in men than women.

What causes acute myeloid leukaemia?

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

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

- Radiation. For example, previous radiotherapy for another condition. Many survivors of the atom bomb used in world war II developed AML caused by the fall out of radiation.
- Past treatment with chemotherapy or other drugs that weaken the immune system.
- Smoking. (A chemical called benzene in cigarettes is thought to be a risk factor for AML.)
- If you have certain conditions of the bone marrow you have an increased risk of developing AML at a later time. These are called myelodysplastic syndromes and myeloproliferative disorders. For example, thrombocythaemia, polycythaemia rubra vera, myelofibrosis, etc.

What are the main symptoms and problems when AML develops?

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

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

The abnormal blasts may also accumulate in other sites. You may therefore develop swollen glands, an enlarged spleen or liver, and occasionally other rare symptoms. Other common symptoms include pain in the bones or joints, persistent fever, and weight loss. Left untreated, AML usually causes death within a few months.

How is acute myeloid leukaemia diagnosed and assessed?

A blood test

A blood test can often suggest the diagnosis of AML. The test will typically show a low number of: red blood cells, normal white blood cells, and platelets. Some blast cells which have spilled into the bloodstream from the marrow are also usually seen. Sometimes large numbers of blast cells occur in the bloodstream. Further tests are usually done to confirm the diagnosis.

A bone marrow sample

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

Cell and chromosome analysis

Detailed tests are done on abnormal blast cells obtained from the bone marrow sample or blood test. The chromosomes within the cells are checked for certain changes. Chromosomes are the parts in the cell which contain DNA - the genetic make-up of the cell. Various sub-types of AML can be diagnosed by detecting changes which occur to parts of one or more chromosome. (These chromosome changes only occur in the leukaemia cells, not the normal body cells.) It is important to know the exact sub-type of AML as the treatments and outlook (prognosis) can vary, depending on the type.

Various other tests

A lumbar puncture is done if symptoms suggest that the abnormal cells have spread to the brain or spinal cord. This test collects a small amount of fluid from around the spinal cord (cerebrospinal fluid - CSF). It is done by inserting a needle between the vertebra in the lower (lumbar) region of the back. The fluid is examined for leukaemia cells. A chest x-ray, blood tests, and other tests are done to assess your general wellbeing.

What is the treatment for acute myeloid leukaemia?

The aim of treatment is to kill all the abnormal cells. This then allows the bone marrow to function normally again, and produce normal blood cells. The main treatment is chemotherapy. A stem cell transplant is used in some cases.

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

- The exact sub-type of AML.
- Your age, sex and general health.
- The number of blasts in the blood at diagnosis.
- How well the condition responds to the initial phase of treatment (see below).
- Whether the leukaemia is a 'secondary' complication from a previous bone marrow problem.
- Whether the leukaemia has spread to the brain and/or spinal cord.

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

Chemotherapy

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

Usually the course of chemotherapy is given in 'cycles'. A cycle is a spell of treatment followed by a rest from treatment. For AML each cycle typically consists of 5-10 days of treatment followed by 3-4 weeks rest. The rest from treatment allows your body to recover from any side-effects, and gives a chance for damaged normal cells to recover before the next spell of treatment.

The length of a full course of treatment is often about six months. So this may consist of about 4-6 cycles of treatment over the six months. But a full course of treatment can vary depending on your circumstances.

Chemotherapy for AML is usually divided into two 'phases'.

- Induction phase. This is the first few cycles of treatment. This aims to kill most of the leukaemia cells. At the end of this phase there is usually no leukaemia cells detectable in a blood sample, or seen in a bone marrow sample. This is called being 'in remission'. Remission does not mean 'cure'. It means that no abnormal cells can be detected by tests.
- Consolidation (Intensification) phase. This is the remaining cycles of treatment and the type of drugs used may be different. This phase of treatment aims to kill any remaining leukaemia cells which may still be present (although not detected by any tests).

Stem cell transplant

A stem cell transplant (SCT) (sometimes called bone marrow transplant) is sometimes used, depending on the type of the AML. For example, it may be used in types classed as 'high risk', and in some cases where the leukaemia has recurred (relapsed) following treatment with usual chemotherapy. (See separate leaflet called '*Stem Cell Transplant*' for more details.)

Supportive treatment

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

Treatment of relapses

Despite treatment, in some cases the AML returns (relapses) sometime after treatment ends. Relapses are treated in a similar way to the initial treatment, but the treatment regime is often more intensive and may include a stem cell transplant.

Side effects from chemotherapy

Side effects during treatment

The drugs used for chemotherapy are powerful and often cause unwanted side-effects. The drugs work by killing cells which are dividing and so some normal cells are damaged too. Side-effects vary from drug to drug and your doctor will advise. The most common side effects are nausea (feeling sick), loss of hair, and an increased risk of infection (as the normal white blood cells are affected by treatment. Anti-sickness drugs are commonly used to prevent nausea.

Late side-effects

In a small number of cases, problems develop months or years after a period of intensive chemotherapy. For example, treatment may affect fertility or the function of certain hormone producing glands. There is also a small increased risk of developing a different cancer later in life.

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

What is the outlook (prognosis)?

In general, the outlook is poor, but it has improved in recent years as treatments continue to improve. It is difficult to give exact figures. However, the chance of a good response to treatment varies. It depends on factors such as the exact type of the AML and your age. For example, for people under the age of 60, there is a good chance of a cure where the AML is classed as low risk.

The outlook is generally not as good for people over the age of 60. This is partly because older people may not be able to tolerate intensive chemotherapy as well as younger people. Also, because some cases in older people are secondary to a previous bone marrow problem, and these tend to respond less well to treatment.

A specialist will be able to give a more accurate prognosis for each individual case.

Further help and information

CancerBACUP

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

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

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

Leukaemia Research Fund

Web: www.lrf.org.uk

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

Leukaemia Care

2 Shrubbery Avenue Worcester WR1 1QH

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

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

Cancer Research UK

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

Other support groups

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