

Chronic Myeloid Leukaemia (CML)

Chronic myeloid leukaemia is a cancer of blood forming cells in the bone marrow. Abnormal cells gradually fill the bone marrow and spill into the bloodstream. The disease typically develops very slowly and symptoms such as anaemia, bleeding problems or infections may not occur for years after the disease starts. Treatment aims to reduce the number of abnormal cells.

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 made in the bone marrow spill out into the bloodstream. There are several types of leukaemia. Most types arise from cells which normal 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.

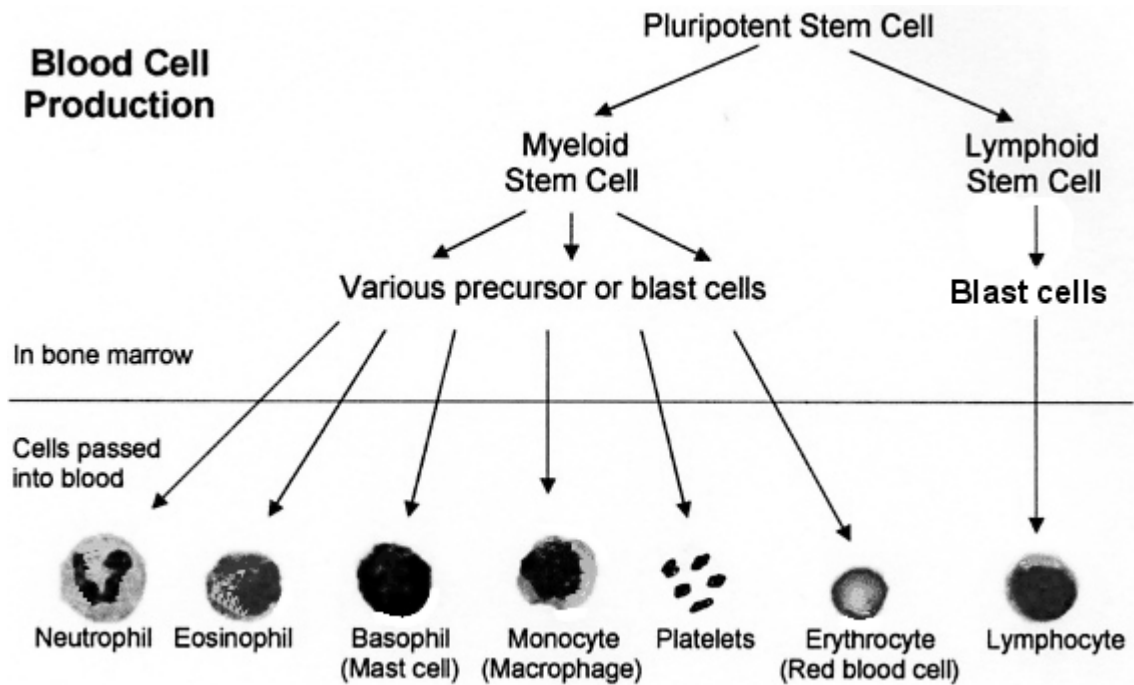
The bone marrow, stem cells and blood cell production

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 chronic myeloid leukaemia.

What is chronic myeloid leukaemia?

CML is sometimes called chronic myelogenous leukaemia, chronic granulocytic leukaemia, or chronic myelocytic leukemia.

CML develops due to a problem with a stem cell in the bone marrow which becomes abnormal. The abnormal stem cell multiplies and the cells that are made from the abnormal stem cells mature and develop into near normal white cells - mainly neutrophils, basophils and eosinophils (collectively called granulocytes). Large numbers of these cells are made in the bone marrow and spill into the bloodstream.

(In contrast, in **acute** myeloid leukaemia (AML) the abnormal cells that are made in large quantities are immature abnormal 'blast cells'. This is quite a different disease to CML - see separate leaflet.)

Typically, CML develops and progresses slowly - over months or years, even without treatment.

Who gets chronic myeloid leukaemia?

Chronic myeloid leukaemia (CML) is the rarest of the four main types of leukaemia. There are less than 1000 cases in the UK each year. It occurs mainly in adults, and becomes more common with increasing age. It is very rare in children. It is more common in men than women.

What causes chronic myeloid leukaemia?

A leukaemia is thought to first start from one abnormal cell. What seems to happen is that certain vital genes which controls how the cell divides, multiplies, and dies are damaged or altered. This makes the cell abnormal. If the abnormal cell survives it may multiply, produce many abnormal cells, and develop into a leukaemia. In the case of CML it is a blood stem cell which is first damaged and affected.

In most cases of CML, the reason why a stem cell becomes abnormal 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 known for CML are high dose radiation (for example, previous radiotherapy for another condition) and exposure to the chemical benzene.

How does CML develop and what are the symptoms?

Typically, CML runs a course of three phases

An initial chronic phase

This phase usually lasts a number of years (often five years or more). During this phase the disease progresses very slowly. You may remain stable, with little or no change in the severity of the disease for long periods. Many people in this phase have no symptoms, or only minor symptoms. CML may be first diagnosed by chance in this phase when a blood test is taken for another reason.

A transformation phase (also known as the accelerated phase)

In time, the disease process tends to speed up and change. In this phase, the number of abnormal cells in the bone marrow and bloodstream builds up. Many of the abnormal cells are 'blast' (immature) white blood cells. As many abnormal cells build up in the bone marrow it is difficult for normal cells in the bone marrow to survive and make enough normal blood cells. Therefore, the main problems and symptoms which tend to develop include:

- Anaemia. This occurs as the number of red blood cells in the bloodstream goes down. This can cause tiredness, breathlessness and other symptoms. You also look pale.
- Blood clotting problems. This is due to low numbers of platelets in the bloodstream. This can

cause easy bruising, bleeding from the gums, and other bleeding-related problems.

- Serious infections. The abnormal white blood cells and blast cells do not protect against infection. If there is a reduced number of normal white blood cells which usually combat infection, there is a risk of serious infections developing.

Other symptoms include: mild pain on the left side of the abdomen caused by a swollen spleen (the spleen may enlarge with abnormal cells), sweats, and weight loss.

The transformation phase typically lasts 3-9 months before passing into the third blast phase. Sometimes the chronic phase goes directly into the blast phase with no intermediate transformation phase.

A third 'blast' phase

In this phase the condition rapidly gets worse and behaves like an acute leukaemia. Many immature 'blast' cells develop and fill much of the bone marrow and cause worsening of symptoms described above. Many blast cells spill out into the bloodstream and the blast cell count in blood tests is high.

How is chronic myeloid leukaemia diagnosed?

A blood test

A blood test typically shows changes in the number and pattern of white blood cells. This suggests the diagnosis of CML. A bone marrow biopsy is then usually done to confirm the diagnosis. In the accelerated and blast phase, the number of blast cells seen in the blood sample (the 'blast cell count') also increases.

A bone marrow sample

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

Cell and genetic tests

Detailed tests are done on the abnormal 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. In most cases of CML the abnormal cells contain a change in chromosome 22. This changed chromosome is shortened and is called the 'Philadelphia chromosome'. An abnormal gene called bcr/abl is made on the abnormal chromosome 22. This gene is likely to be responsible for the abnormal cancerous behaviour of each abnormal cell. (These chromosome changes only occur in the leukaemia cells, not the normal body cells.) Some rarer sub-types of CML do not have the Philadelphia chromosome.

Various other tests

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

What is the treatment for chronic myeloid leukaemia?

Treatment for the initial chronic phase

The aim of treatment is to control the disease process, to ease any symptoms, and to prevent (or delay) the progression into the further two stages. You may be advised to have one or more of the following treatments.

- **Interferon alpha.** This is a chemical which naturally occurs in the body. It normally helps to combat viral infections. It has also been shown to help the immune system to combat cancer and leukaemia cells. Interferon can now be made and is given as a treatment for various conditions including CML. It is normally given by a small injection under the skin several times a week. Most people learn how to do this themselves.

- **Imatinib (Glivec) tablets.** This drug is known as a 'tyrosine kinase inhibitor'. The chemical tyrosine kinase is made by the abnormal gene Bcr/abl on the 'philadelphia' chromosome described above. This is thought to be responsible for the abnormal growth and behaviour of the abnormal cells. Imatinib works by blocking the effect of tyrosine kinase.
- **Chemotherapy tablets.** 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.) In the chronic phase of CML, tablets taken by mouth each day called hydroxyurea is the usual chemotherapy drug used. Another drug called arabinoside is also sometimes used to treat CML.
- **A stem cell transplant** (sometimes called bone marrow transplant) is sometimes an option in younger patients with CML. This may be curative. See separate leaflet called '*Stem Cell Transplant*'.

Treatment for transformation and blast phases

Treatment is usually with more intensive chemotherapy than is given for the chronic phase. This usually means a combination of chemotherapy drugs given directly into a vein (intravenous chemotherapy). Imatinib (Glivec) tablets may also be used.

Supportive treatment

Other treatments include antibiotics or antifungal drugs if infection occurs and blood transfusions to counter low levels of red blood cells and/or platelets.

What is the outlook (prognosis)?

Overall, the outlook is reasonably good. Treatment in most cases is not curative but treatment often keeps the disease under control for a number of years. A successful stem cell transplant in people who have this treatment is the only means of a permanent cure. Your specialist will be able to give a more accurate prognosis for your particular circumstances.

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.

Other support groups

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