

Chronic Lymphocytic Leukaemia (CLL)

Chronic lymphocytic leukaemia is a condition where you build-up many abnormal lymphocytes (white blood cells). It occurs mainly in people over 60. It typically develops very slowly and symptoms such as anaemia, bleeding problems or infections may not occur for years after the disease starts. Treatment, when needed, aims to reduce the number of abnormal lymphocytes.

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 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.

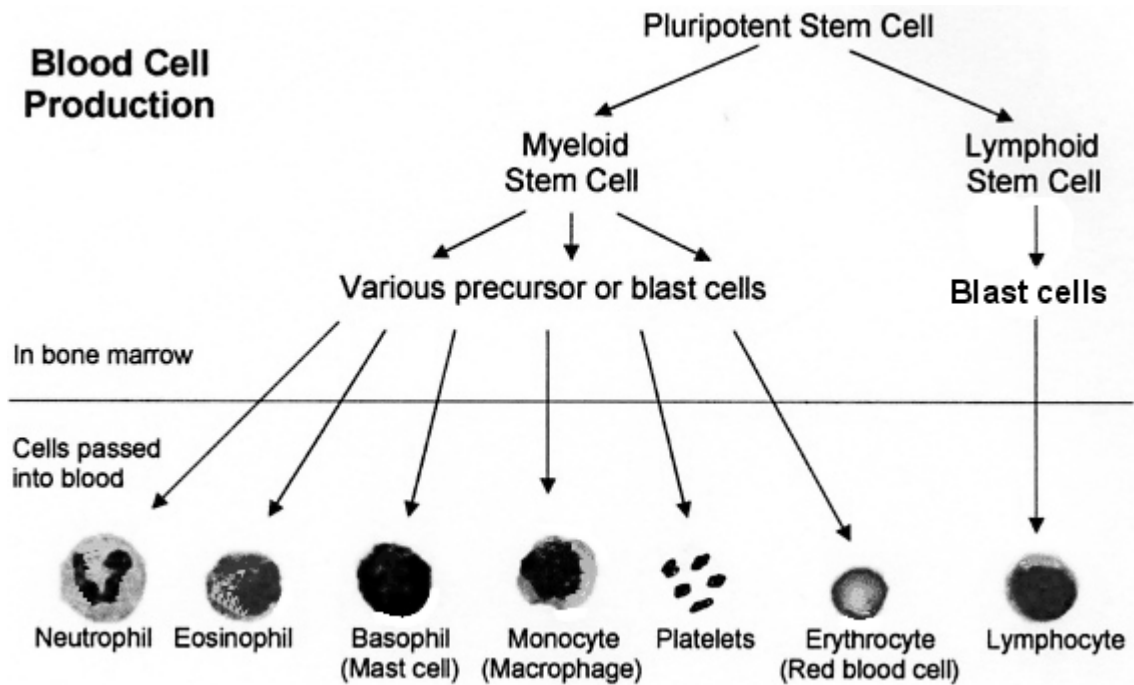
The bone marrow, stem cells and blood cell production

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 chronic lymphocytic leukaemia.

What is chronic lymphocytic leukaemia?

Chronic lymphocytic leukaemia (CLL) is a condition where you have many abnormal B-lymphocytes. The lymphocytes look normal under a microscope, but are abnormal as they do not function properly. The main reason for the build-up of the abnormal lymphocytes is because they live too long - they do not die after the usual lifespan of a lymphocyte. (This is different to the acute types of leukaemia where the cells rapidly multiply 'out of control'. In CLL the abnormal lymphocytes are not thought to multiply faster than normal lymphocytes.) Typically, CLL develops and progresses very slowly - over months or years, even without treatment.

Who gets chronic lymphocytic leukaemia?

CLL is the most common type of leukaemia. It occurs in about 3 in 100,000 people each year. Most cases occur in people over at the age of 60. It is rare under the age of 40.

What causes chronic lymphocytic 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 and develop into a leukaemia. However, it is not known what causes the damage which leads to abnormal lymphocytes developing into CLL.

What are the symptoms and problems with CLL?

At first, in many cases, there are no symptoms. The condition is often first diagnosed by chance when a blood test is taken for another reason. Over months or years, a large number of abnormal lymphocytes may gradually build up in the bloodstream without causing any problems.

In time, the abnormal lymphocytes may fill much of the bone marrow. Because of this, it is difficult for normal cells in the bone marrow to survive and make enough normal blood cells. Therefore, the main problems which may eventually 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 lymphocytes 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.

The abnormal lymphocytes may also build-up in lymph glands and in the spleen. With CLL it is also common to develop swollen glands in various parts of the body, particularly in the neck and armpits, and develop an enlarged spleen. Other common symptoms include: persistent fever, night sweats, and weight loss.

Some people with CLL also have an associated auto-immune disease

Lymphocytes normally make antibodies to attack bacteria, viruses, and other 'germs'. In people with auto-immune diseases, the immune system also makes antibodies against part or parts of the body. About 1 in 8 people with CLL make antibodies against red blood cells and/or platelets. This can destroy red cells and platelets. This can lead to anaemia and bleeding problems, or make anaemia and bleeding problems worse if the CLL is already causing these problems.

Transformation of CLL

In about 1 in 6 cases, the CLL changes at some point (transforms) to a more 'acute' form of leukaemia. This then progresses more rapidly and responds less well to treatment. If this occurs, symptoms may rapidly become worse.

How is chronic lymphocytic leukaemia diagnosed and assessed?

A blood test

A blood test typically shows a large number of lymphocytes. These look normal under the microscope so further tests are needed to confirm the diagnosis.

Cell typing (Immunophenotyping)

Detailed tests are done on the lymphocytes obtained from the blood test (or bone marrow sample). These help to confirm the diagnosis of CLL and to rule out other rarer related disorders. Some more detailed tests of the genes in the lymphocytes are being developed. These will help to subdivide CLL into different categories. This may help to predict which cases will develop into the more severe type of disease, and help to guide decisions about treatment.

A bone marrow sample

This test is not always necessary to diagnose CLL. It may be done to confirm the diagnosis and rule out other conditions. 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. 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.)

Various other tests

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

Staging chronic lymphocytic leukaemia

The severity of CLL is commonly assessed by the following staging system.

- Stage A - there are less than three areas in the body with swollen lymph glands.
- Stage B - there are three or more areas in the body with swollen lymph glands.
- Stage C - there is a low number of red cells (anaemia), a low number of platelets, or both.

What is the treatment for chronic lymphocytic leukaemia?

Treatment for stage A (early stage)

Many people with stage A CLL do not need any treatment. This is because many people with stage A disease do not have any symptoms, and it often causes little harm. In many cases of stage A disease, the disease progresses slowly and never needs treatment. For people in stage A CLL the risks of treatment often outweigh the benefits of treatment. Treatment may be started if symptoms develop, or when blood tests show that the disease is progressing more rapidly. Your specialist will advise on the pros and cons of treatment, and when it should be started.

However, it is important to have regular checks to detect if the CLL has progressed to stage B or C when treatment is then commonly advised.

Treatment for Stage B and C (later stages)

The aim of treatment is to kill the abnormal cells. This then allows the bone marrow to function normally again, and produce normal blood cells. The main treatment is chemotherapy. Other forms of treatment are sometimes used.

- Chemotherapy is a treatment which uses anti-cancer drugs to kill cancer (leukaemia) cells, or to stop them from multiplying. (There is a separate leaflet which gives more details about chemotherapy.) For the CLL, the chemotherapy is usually taken as tablets which you take each day. Sometimes chemotherapy drugs are given by injection.
- Monoclonal antibodies are a treatment which are sometimes used to treat CLL. (For example, products called alemtuzumab and rituximab.) Monoclonal antibodies are small proteins and are different to normal chemotherapy. They work by attaching to the abnormal lymphocytes which destroys them without harming other cells. Monoclonal antibodies may be used in addition to chemotherapy.

- Radiotherapy may be used to reduce the size of enlarged lymph glands or spleen.
- Steroid tablets are sometimes added to the treatment. They may help the chemotherapy drugs to work better. Steroids also help to control auto-immune complications which occur in some cases (described above).

The treatments described above do not cure CLL. The above treatments aim to keep you in remission. That is, to keep you with very low levels of abnormal lymphocytes which enables your bone marrow to function normally.

A stem cell transplant (SCT)

A stem cell transplant (sometimes called bone marrow transplant) is sometimes used, especially in younger patients with progressing disease. It involves intense chemotherapy. A successful stem cell transplant can cure CLL as the lymphocytes made by the transplanted stem cells will be normal. (See separate leaflet called '*Stem Cell Transplant*' for more details.)

Supportive treatment

If needed, other treatments include antibiotics or antifungal drugs if infection occurs, and blood transfusions to counter low levels of red blood cells or platelets.

What is the outlook (prognosis)?

Overall, the outlook is reasonably good. Although CLL is not a condition that can usually be cured, many cases are in stage A where the condition is not usually serious, and treatment is not usually needed. Treatment for stages B and C often puts the disease into remission. In general, the average survival of people with stage A CLL is greater than 10 years. Many people live much longer. The outlook for stages B and C is not as good as stage A but most people live several years after the diagnosis of CLL is first made. Your specialist will be able to give a more accurate prognosis for your particular circumstances.

Also, you have to bear in mind that most people with CLL are over the age of 60. CLL tends to be a slowly progressing disease which can last for years. Many people with CLL die of other unrelated conditions which affect older people.

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.