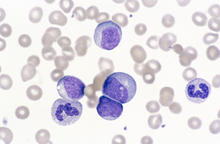
Leukaemia: how can stem cells help?

[](http://www.eurostemcell.org/files/factsheets/Chronic_myeloid_leukaemia_Wellcome_crop.jpg)

Leukaemia is among the first diseases to have been treated using stem cells - bone marrow transplants contain blood stem cells and can save lives. But many difficulties remain. Ongoing research aims to increase our understanding of the disease and improve treatments. How are stem cells helping  patients today, and what are the possibilities for the future?

About leukaemia

Leukaemia is a cancer of the blood and bone marrow. It causes white blood cells (also called leukocytes) to develop abnormally. White blood cells are made in the bone marrow and their main job is to defend the body against infection and disease. In most forms of acute leukaemia the body produces large numbers of abnormal white blood cells which look like immature cells called blasts. These leukaemic blasts accumulate in the bone marrow and suppress the formation of normal white blood cells.

Leukaemias are grouped according to the severity of the disease (how fast it is growing) and the types of white blood cells affected:

* **Acute leukaemias** are rapidly growing leukaemias that develop very quickly and cause a sudden increase in the number of malignant (cancerous) immature white blood cells. They are usually sub-classified as acute lymphoblastic leukaemia (ALL) or acute myeloid leukaemia (AML) depending on the types of white blood cells that are affected.
* **Chronic leukaemias** are more slowly developing leukaemias that may escape diagnosis for several years before they are detected. They are usually sub-classified as either chronic lymphocytic leukaemia (CLL) or chronic myeloid leukaemia (CML).
* There are also less common types and subtypes of leukaemia.

What causes leukaemia?

Like most cancers, leukaemias are caused by a series of rare mutations (changes) in the genes inside certain cells. Occasionally, one of these mutations may be inherited and then the individual is predisposed to develop leukaemia. Other known causes include accidental exposure to radiation and treatment with some types of anti-cancer drugs. However, most leukaemias are caused by an accumulation of mutations that occur naturally - mistakes which happen during the production of new cells in the body. A large number of gene mutations have been linked to human leukaemias, but in most cases it is not yet known which ones really drive the disease. Chronic myeloid leukaemia (CML) is caused by a single genetic change but most other leukaemias appear to be more complicated and may involve combinations of mutations.

Many types of leukaemia are thought to originate in blood stem cells, also called haematopoietic stem cells (HSCs). HSCs are responsible for making new blood cells in our bodies all our lives. If a stem cell is affected by genetic changes, all the cells it produces will inherit the same mutation. It has been shown that CML starts with a particular mutation in HSCs. However, cells go through a number of steps to develop from HSCs into specialised cells such as white blood cells. Mutations might happen at any of these steps. For many leukaemias, a complex series of events is probably involved and it is not yet clear where the first important mutation occurs.

How are healthy blood stem cells used to treat leukaemia?

Acute leukaemia usually requires immediate and intensive treatment. Depending on the particular type of leukaemia and many other things about the individual patient, treatment options might include chemotherapy, steroids or a more intensive procedure such as a haematopoietic stem cell transplant combined with high-dose chemotherapy.

High-dose chemotherapy is the most effective currently established method to kill leukaemic cells and can cure some patients. However, it also severely damages the remaining normal blood-forming cells in the bone marrow. To replace these cells, patients are given a haematopoietic stem cell transplant (HSCT). The cells for the transplant can be collected from the blood or bone marrow of a healthy donor. In fact, the transplant includes not only HSCs, but also important immune cells that help to kill leukaemic cells. A patient’s own cells can sometimes be used for the transplant, if it is possible to collect enough healthy cells before the treatment is performed. If a different donor is needed, they must [match the patient’s tissue type](http://www.macmillan.org.uk/Cancerinformation/Cancertreatment/Treatmenttypes/Stemcellbonemarrowtransplants/Allogeneic%28donor%29stemcelltransplants/Generalinformation/Findingadonor.aspx) otherwise the transplanted donor cells will be attacked by the patient’s immune system and rejected.

HSCTs are particularly effective for treating certain types of acute leukaemia. However, the procedure is intensive and risky with the potential for substantial after effects. Therefore, this type of stem cell transplant is only considered when standard-dose chemotherapy fails to eradicate the disease.

Limitations of current stem cell treatments

A haematopoietic stem cell transplant using cells from a donor can have serious side effects:

**Infections** - The transplanted stem cells need time to produce the necessary new blood cells for the body. Infections can occur due to the inevitable delay in the replenishment of the patient’s immune system with white blood cells, which leaves the patient highly vulnerable to infections for a period. Careful observation and preventative treatment with antibiotics can help to reduce infection risks.

**Graft-versus-host disease** (GvHD) – This complication occurs when donor blood cells attack the patient’s tissue. Symptoms include rashes, diarrhoea, blisters and fever. GvHD is a serious complication and can be life-threatening. It can be minimized by closely matching the tissue type of the donor to the patient. This is easiest to achieve if the patient has a matched sibling. Other strategies to prevent GvHD include suppressing the immune system with drugs and removing a specific type of white blood cells (lymphocytes) from the transplant.

Researchers and doctors are investigating ways to improve current transplantation approaches in order to address these limitations.  Another challenge is the shortage of donors and several organisations are working to increase the number of volunteers in donor registries.

Recent developments and current research on haematopoietic stem cell treatments for leukaemia

The high dose of chemotherapy given to leukaemia patients before a transplant destroys both leukaemic cells and healthy bone marrow cells. Newer forms of transplantation called mini-allografts or reduced-intensity allografts have been developed to reduce the risk. These procedures allow lower doses of chemotherapy to be used, which helps avoid extensive damage to the bone marrow. Instead, donor immune cells are transplanted with the donor haematopoietic stem cells to attack and eliminate any remaining leukaemic cells. This is called a **graft-versus-leukaemia** effect. This type of transplant has fewer side effects but some serious ones remain, particularly GvHD.

There are several new techniques which may help to prevent GvHD and these are currently being tested in the clinic. Certain types of immune cells (regulatory T lymphocytes) that have a suppressive effect on the immune system may be administered to the patient. This can help prevent the donor immune cells from attacking the patient’s own cells. Alternatively, attempts are being made to selectively remove the immune cells that cause GvHD from the transplant.

Scientists and doctors are also currently investigating treatments that might reduce the time it takes for the patient’s immune system to recover after a haematopoietic stem cell transplant. One option is to treat the patient with selected proteins called growth factors, which can enhance the production of the particular immune cells needed to fight infections. This can help reduce the risk of infection while the patient recovers.

The future of haematopoietic stem cell treatments for leukaemia

Stem cell research is a rapidly developing field. New technologies such as [induced pluripotent stem cells](http://www.eurostemcell.org/factsheet/reprogramming-how-turn-any-cell-body-pluripotent-stem-cell) are already being used to study leukaemia in the lab. They provide a tool for producing large numbers of leukaemic cells in a dish. Researchers can then study the cells to learn more about how the disease works and to design new drug therapies. In the future, new methods for the lab-based production of haematopoietic stem cells and their use in transplantation may also become available. This could help with the shortage or bone marrow donors for transplants. Today, chemotherapy combined with transplantation of HSCs from either the patient or a donor offers life-saving treatment for severely ill leukaemia patients.

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