Allogeneic Stem Cell Transplants

A Guide for Patients

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

A stem cell transplant is a procedure which involves replacing your faulty or damaged bone marrow cells. Allogeneic means that the stem cells you receive come from a donor. This booklet helps you to understand this treatment a little better.

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If you need specific advice or are concerned about anything regarding stem cell transplants, please contact your medical team or Clinical Nurse Specialist (CNS).

If you would like any information on the sources used for this booklet, please email **communications@leukaemiacare.org.uk** for a list of references.

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In this booklet

About Leukaemia Care

Leukaemia Care is a national charity dedicated to ensuring that people affected by blood cancer have access to the right information, advice and support.

Our services

Helpline

Our helpline is available 9.00am - 10.00pm on weekdays and 9.00am - 12.30pm on Saturdays. If you need someone to talk to, call **08088 010 444**

Nurse service

We have two trained nurses on hand to answer your questions and offer advice and support, whether it be through emailing **nurse@leukaemiacare.org.uk**, over the phone on **08088 010 444** or via LiveChat.

Patient Information Booklets

We have a number of patient information booklets like this available to anyone who has been affected by a blood cancer. A full list of titles – both disease specific and general information titles – can be found on our website at **www.leukaemiacare.org.uk/resources/filter-by-resource-type/information-booklets**

Support Groups

Our nationwide support groups are a chance to meet and talk to other people who are going through a similar experience. For more information about a support group local to your area, go to **www.leukaemiacare.org.uk/our-support-groups**

Buddy Support

We offer one-to-one phone support with volunteers who have had blood cancer themselves or been affected by it in some way. You can speak to someone who knows what you are going through. For more information on how to get a buddy call **08088 010 444** or email **care@leukaemiacare.org.uk**

Online Forum

Our online forum, **www.healthunlocked.com/leukaemia-care**, is a place for people to ask questions anonymously or to join in the discussion with other people in a similar situation.

Patient and carer conferences

Our nationwide conferences provide an opportunity to ask questions and listen to patient speakers and medical professionals who can provide valuable information and support.

Website

You can access up-to-date information on our website, **www.leukaemiacare.org.uk**, as well as speak to one of our care advisers on our online support service, LiveChat (9am-5pm weekdays).

Campaigning and Advocacy

Leukaemia Care is involved in campaigning for patient well-being, NHS funding and drug and treatment availability. If you would like an update on any of the work we are currently doing or want to know how to get involved, email **advocacy@leukaemiacare.org.uk**

Patient magazine

Our free quarterly magazine includes inspirational patient and carer stories as well as informative articles by medical professionals. To subscribe go to **www.leukaemiacare.org.uk/resources/subscribe-to-journey-magazine**

What are stem cells?

Stem cells are blood-forming cells that reside in your bone marrow, the soft tissue inside the bones.

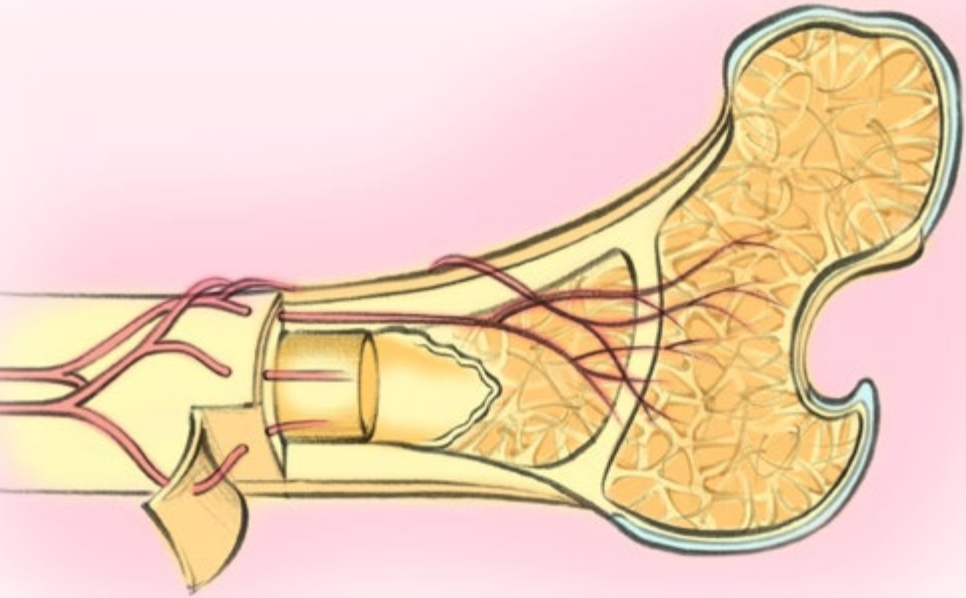
Stem cells can mature to become one of three types of blood cell:

- Leukocytes (white blood cells), which fight infection;
- Red blood cells, which carry oxygen;
- Platelets, which help the blood to clot.

Stem cells also have the ability to self-replicate into identical copies; these cells are therefore preserved throughout life to assure a constant supply of blood cells.

The process of the development and maturation of stem cells is known as haematopoiesis. Every day, haematopoietic stem cells produce billions of new blood cells. If haematopietic stem cells are damaged and unable to perform this function, life expectancy without medical intervention is only a few months.

Haematopoietic stem cells are found in the bone marrow, peripheral blood and the umbilical cord. Cells from any of these sources can be used for transplantation.



What are stem cell transplants?

Haematopoietic Stem cell transplantation (HSCT) is a medical procedure used to replace your faulty or damaged bone marrow cells for healthy ones from a donor.

HSCT is a common approach nowadays for treating blood conditions, including non-malignant and malignant diseases:

- Non-malignant diseases, in which your bone marrow cannot produce blood cells, or the cells produced are defective. This often causes abnormally low or high numbers of blood cells (leukocyte, red blood cell or platelet) in the circulation.
- Malignant (neoplastic) diseases, which include blood cancers such as leukaemia, lymphoma or multiple myeloma.

If you are diagnosed with a blood cancer or some other blood disorder, your blood cell production may be impaired, resulting in over or underproduction of blood cells. As a consequence, your system may no longer be able to perform some of its functions, such as fighting infection or transporting oxygen to organs and tissues.

Haematopoietic stem cell transplants are performed to control or cure some of these diseases.

Depending on the donor, there are two general types of stem cell transplants:

1. **Autologous, also known as auto transplant** - If you are having an autologous stem cell transplant it means that you donate your own stem cells before receiving high-dose chemotherapy. These cells are administered back to you afterwards to rescue your bone marrow.
2. **Allogeneic** - In this case, you receive stem cells from a healthy donor.

The booklet talks about allogeneic stem cell transplants. If you would like more information about autologous stem cell transplants, please request a copy of our other stem cell booklet from the care team at **08088 010 444** or email **care@leukaemiacare.org.uk**

Who receives a stem cell transplant?

Some non-malignant blood diseases can be treated with the use of drugs that help control the excessive activity of the immune system responsible for the disease.

On the contrary, neoplastic blood diseases (blood cancers) often require chemotherapy, with or without radiotherapy. In some patients chemotherapy will be sufficient to control the disease. In other cases, chemotherapy is not enough; and a stem cell transplant (autologous or allogeneic) is required.

If you have been diagnosed with a blood disorder, your doctor will explain the different treatment options with you, and decide which treatment intervention is appropriate depending on your condition, the therapeutic objectives, and the availability and source of stem cells.

Allogeneic transplantation is performed with haematopoietic stem cells from a healthy donor. This modality of transplantation is indicated for diseases that originate either in your stem cells or in some of the blood cell lineages derived from them, including:

- **Leukaemias and lymphomas** – characterised by neoplastic transformation and abnormal production of white blood cells.
- **Medullary aplasia and Fanconi's syndrome** – diseases characterised by a lack of stem cells in the bone marrow.
- **Congenital and acquired neutropenia and thrombocytopenia** – characterised by a lack of production of any of these cell lineages.
- **Congenital and acquired immunodeficiencies** - characterised by the lack or malfunctioning of immune cells.

In all cases, the indication for one type of transplant or other transplantation should be individualised. Your doctor will evaluate both your disease and the possible risks and benefits of Haematopoietic stem cell transplant and other therapeutic measures.

Types of stem cell transplants

Type of transplant	Aim of transplantation	Advantages	Disadvantages
Autologous	Rescue bone marrow function after high-dose chemotherapy	Lower risk of post-transplant complications	Greater chance of relapse
Allogeneic	Replace damaged cells in bone marrow for healthy ones, combining the effects of chemotherapy and donor cells to destroy residual malignant cells	Lower risk of relapse	Greater risk of post-transplant complications

Allogeneic transplants

In an allogeneic stem cell transplant, you are given high-dose chemotherapy, with or without radiotherapy, followed by a transplant of healthy stem cells from a sibling, a relative or from an unrelated donor.

Healthy donor cells have been seen to contribute to the elimination of residual leukaemic cells in the patients, reducing the risk of relapse. This beneficial effect is called the graft-versus-leukaemia (GVL) or graft-versus-tumour effect, and is due to the action of donor T lymphocytes attacking and eliminating any neoplastic cells in the patient.

Unfortunately, if you are having an allogeneic transplant, the T lymphocytes from the donor will also recognise your own cells as foreign, and may trigger an immunological attack against your healthy tissues; this adverse event is known as graft-versus-host disease (GVHD; see page 31).

GVHD can be minimised when there is a good compatibility between you and your donor. This

compatibility is valued through the study of Human Leukocyte Antigen (HLA) proteins located on the surface of most cells in your body. HLA proteins are the main way the immune system tells the difference between your own and foreign cells, and the degree of HLA matching between you and your donor is the single most significant factor contributing to a successful transplant.

To perform a HLA compatibility study, both you and your donor must provide a blood or saliva sample. The samples are analysed and compared in the laboratory to identify which donor has an HLA signature in their cells more similar to yours.

A large number of HLA antigens have been identified, and the five most important are the so-called A, B, C, DRB1 and DQB1, of which we inherit one from our father and another from our mother; making it a total of 10 antigens.

Sibling transplants

Since every individual inherits half of HLA antigens from their father and the other half from their mother, the probability to find a compatible donor with a good HLA match is greater among siblings. If you have a sibling as a potential donor, to consider them as compatible with you for stem cell transplant purposes, you must both demonstrate six HLA antigens (2A, 2B and 2DRB1).

Due to the laws of genetic inheritance, one in four siblings (25%) will be fully compatible with the patient, so the probability of your finding a family donor increases with the number of siblings.

Matched Unrelated Donor (MUD) transplants

This is a standard modality for allogeneic transplantation in which a non-family donor must be found, searching in national and international stem cell registries. An ideal donor will be 100% compatible with you (10 out of 10 HLA identity), however donors with 90% compatibility (9 out of 10 HLA identity) are also suitable.

Matched Unrelated Donor transplants increase the chance of

Types of stem cell transplants (cont.)

you finding a stem cell donor.

Haploidentical transplants

If you need a stem cell transplant but do not have a compatible sibling or matched unrelated donor, medical advances have allowed using haploidentical related donors. A haploidentical donor is a 50% HLA match between you and your donor. In these cases the donor may be any of your parents, brothers and sisters or your children.

In the past, haploidentical transplantation was a very complex transplant modality, rarely performed because of the high risk of severe GVHD. In spite of this, methods have now developed to overcome this risk, by eliminating the donor T lymphocytes responsible for GVHD prior to the transplant, and by improving the treatments available for GVHD.

Although it is still an experimental transplant modality, these advances have made haploidentical transplants an ever growing option for patients who do not have a compatible donor, or in cases in which there is insufficient time for an international search or a suitable cord blood unit is not available.

Syngeneic transplant

In this type of allogeneic transplantation, the donor is your identical twin (coming from the same ovule, which should be distinguished from twins from two ova). Consequently only a limited number of patients benefit from this transplant modality.

The procedure is the same as for any other allogeneic transplantation; however, there will be no GVL or GVHD effects or rejection of the graft, given the total identity between the donor's and your own cells. For this reason, syngeneic transplantation carries a lower risk of complications, but a greater risk of disease relapses after transplantation.

Cord blood transplants

Umbilical cord blood was once discarded as waste material, but it has now become a valuable source of stem cells. Cord blood has a higher enrichment of stem cells than bone marrow or peripheral blood.

For obtaining cord blood stem cells, around 40–70 millilitres (the equivalent of a small cup of coffee) of umbilical cord blood is collected immediately after the cord is clamped and cut. The placenta is separated, and the umbilical cord blood cells are collected into a sterile collection set, from which the blood is drained. Each of these units containing stem cells is cryopreserved and stored in a cord blood bank.

Because umbilical cord contains relatively immature cells, these are not necessary to be as HLA compatible with you as when using stem cells from bone marrow or peripheral blood. This fact facilitates the location of sufficiently compatible cord bloods, making it an attractive possibility if a matched related or unrelated donor cannot be found.

Cord blood transplantation is an easy and safe procedure. There is reduced potential for viral transmission from the donor, and the relative immaturity of the immune cells reduces your chances of experiencing GVHD. The main problem of this transplant modality is that umbilical cord blood contains fewer cells, which may delay the haematologic recovery if you are an adult. Since you will take longer to start producing new blood cells compared to other transplant options, you may have an increased risk of infections in the first few months after your transplant.

The possibility of having a stem cell transplant to treat your disease relies on the availability of a suitable stem cell donor. The greater the immunological compatibility (HLA identity) between you and the donor, the

How is a stem cell donor found?

lower the risk of experiencing complications after the transplant. Therefore, in theory, your ideal donor would be an identical twin (syngeneic transplant). In this case, there would be no risk of your body rejecting the graft or experiencing GVHD; however, you would not benefit from the antileukaemic effect of the graft either, thus increasing the risk of relapse after the transplant.

In neoplastic diseases, a matched sibling will be preferred as your donor, however only about 30% of patients who require an allogeneic transplant have a matched sibling donor. For the remaining patients, a matched-unrelated donor, a haploidentical related donor or a cord blood unit must be found.

If you require a donor urgently, and a suitable unrelated match cannot be found, haploidentical and cord blood transplantation are preferred. Cord blood can be obtained promptly because it is cryopreserved and in inventory in cord blood banks, whereas haploidentical family members need to be willing to donate.

If you have more than one donor (family or non-relative) fully compatible with your HLA system, a series of criteria is followed for the selection of the most suitable one, including:

- Younger donors are usually preferred.
- Male donors are preferred over female donors, regardless of the patient's sex.
- An attempt is made to locate a donor with a weight similar to your own, and having the same blood group (although this aspect is not essential).

CMV compatibility

If a cord blood transplant is chosen, the degree of HLA compatibility is less relevant and the focus is on getting cord blood units with the maximum possible number of stem cells.

The NHS Cord Blood Bank was set up in 1996 to collect, process, store and supply cord blood; it is a public cord blood bank and part of the NHS. There is no charge to the

donor but the product is not stored specifically for that person or their family. The potentially life-saving product is stored indefinitely for a possible transplant.

If you need a cord blood stem cell transplant, your donor cells will most likely come from there.

How to prepare for a stem cell transplant

Haematopoietic stem cell transplant is a complex and long procedure involving different phases, before and after the transplant. Generally speaking, there are five stages:

1. **Tests and examinations** – To assess your general level of health and fitness.
2. **Harvesting** – The process of obtaining the stem cells for the transplant; these will be from a donor.
3. **Conditioning** – The treatment that you receive to prepare your body for the transplant.
4. **Transplanting the stem cells**
5. **Recovery** – You must stay in hospital for at least a few weeks after the transplant.

Stage 1: Tests and examinations

Before you have a stem cell transplant your medical team needs to perform some tests to ensure you are fit enough to undergo the process. This usually takes a couple of days, and the tests might include:

- **X-ray and/or computerised tomography (CT) scan** - These are imaging techniques to check the condition of your organs such as the lungs and liver.
- **Blood tests** - To check your blood cell counts and the levels of a number of biomarkers indicative of liver and kidney function.
- **Electrocardiogram (and, occasionally, echocardiogram)** - An electrocardiogram is a simple test to check your heart's rhythm and electrical activity using sensors attached to your skin. An echocardiogram is a scan to look at your heart and nearby blood vessels.
- **Dental checkup** - Any decaying tooth can potentially be a source of infection during your transplant so it important to have them checked.
- **Respiratory, and gynaecologic and other tests** - You may also have these tests among any

others that your doctor may consider necessary depending on your type of transplant and individual characteristics.

If you have a blood cancer (e.g. leukaemia or multiple myeloma) your doctor will perform a bone marrow biopsy, where a small sample of cells is removed from the hip for analysis.

Stage 2: Harvesting stem cells

If you are having allogeneic transplantation, the stem cells are harvested from the donor and given directly to you without needing to store them.

Stem cells can be harvested from peripheral blood or from the bone marrow. Alternatively, stem cells can also be obtained from umbilical cord blood.

Collecting stem cells from blood

Nowadays, stem cells from the peripheral blood, rather than from the bone marrow, is the most common source for transplantation. This involves taking blood and separating out the stem cells. To boost the number of stem cells in the blood, the donor is given a subcutaneous injection, called Granulocyte-Colony-Stimulating-Factor (GCSF) for a few days (the number of days depends on the regime you or your donor are on) to stimulate the production of stem cells. On the day of the peripheral blood stem cell collection, a blood test is carried out to check whether there are enough circulating stem cells in the blood. In order to collect the stem cells, the vein in each arm will be connected by tubes to a cell-separator machine. Blood is removed from one arm and passed through a filter, before being returned to the body through the other arm. This procedure is not painful and is done while the donor is awake. It takes around three hours and may need to be repeated the next day if not enough stem cells were obtained the first time.

Collecting stem cells from bone marrow

An alternative method of collecting donor stem cells is to remove bone marrow from the hip using a needle

How to prepare for a stem cell transplant (cont.)

and syringe. One needle is inserted usually on each side of the hip, to ensure enough bone marrow is obtained. This is done under a general anaesthetic, so no pain is felt while the procedure is carried out. The area where the needle is inserted may be painful afterwards and leave marks on the skin.

Stage 3: Conditioning treatment

Your conditioning treatment consists of chemotherapy, with or without radiotherapy, given to eliminate as many diseased cells as possible and to prepare your body for receiving the stem cells that will be transplanted soon after.

The dose of chemotherapy is calculated according to your weight. Generally, the drugs are administered intravenously through a central venous line, a thin tube inserted into your chest. This central line stays in place throughout your treatment, making it easier for your medical team to administer drugs.

Conditioning treatment is typically given during the week before your transplant.

The type of conditioning chemotherapy is decided upon your type of disease, age and general health. In few special cases, such as children with severe immunodeficiencies, conditioning treatment may not be necessary and the stem cell transplant is carried out without previous preparation.

Depending on their intensity, conditioning regimens are classified, from more to less intense, as high-dose (myeloablative), reduced-intensity, and non-myeloablative. Your doctor will discuss with you the best option for your particular case.

High-dose (myeloablative) conditioning

This was the first type of conditioning treatment developed for bone marrow transplantation. Myeloablative conditioning is used for removing the abnormal cells from your body, to create space in your bone marrow for the new cells and to avoid your immune system rejecting the transplanted cells.

The dose of chemotherapy used in this modality of conditioning treatment is strong enough

to kill your bone marrow cells (myeloablation); so you need a stem cell transplant to recover your ability to generate new blood cells (this is called haematopoietic rescue).

As part of your conditioning treatment you may also need radiation therapy over the whole body (total body irradiation). Radiation is given fractionally over three to six sessions, administered in three to four days. If you are given total body irradiation special measures are taken to protect your lungs from radiation.

Reduced intensity conditioning (RIC)

In this modality of conditioning treatment you receive a combination of chemotherapeutic and immunosuppressive agents. Chemotherapeutic agents target and eliminate the cells that cause your disease. Unlike myeloablative conditioning, the dose of chemotherapy in reduced intensity conditioning is high enough to kill some but not all the cells in your bone marrow, and blood-cell production could eventually resume even in the absence of a transplant.

You are also given immunosuppressive therapy to lessen the activity of your own immune system, such that it doesn't attack the cells from the donor when infused.

With RIC, your cells and the cells from the donor cohabit in your bone marrow for a certain period of time (this is called mixed chimerism), until the cells of the donor gradually and completely replace your own (this is called complete chimerism). During this process, the cancerous cells that caused your disease are also destroyed by the donor's T lymphocytes (graft-versus-leukaemia effect).

Non-myeloablative conditioning

In non-myeloablative transplants you are only given immunosuppressive agents, so your bone marrow function is practically unaltered.

Reduced-intensity and non-myeloablative conditioning treatment are indicated for specific blood diseases, and also when you have already received a previous transplant (autologous or allogeneic) or if, because of your age or associated

How to prepare for a stem cell transplant (cont.)

diseases (comorbidities), you cannot be treated with aggressive myeloablative conditioning.

Stage 4: Transplant

Your transplant will usually take place a day or two after conditioning has finished. The stem cells are infused slowly into your body through the same central line used for giving you drugs, and the process usually takes between 30 minutes and an hour. The transplant is not painful and you will be awake throughout.

You can find a more detailed description of what happens on transplant day on page 21 of this booklet.

Stage 5: Recovery

After the transplant, you may need to stay in hospital for at least a few weeks, until the infused stem cells settle in your bone marrow and start producing new blood cells. Alternatively, some patients may be discharged within a few hours and will be treated as an outpatient every day for assessment.

During this period, you can experience a number of side effects such as vomiting, diarrhoea and loss of appetite, and it is important to try and prevent infection as much as possible. You are likely to stay in a sterile, germ-free room to prevent infections, and have regular red blood cell and platelet transfusions. If you have visitors, they may need to wear protective clothing, such as an apron and gloves, and they will need to wash their hands before entering the room.

You will usually leave hospital one to three months after the transplant, but may need to stay longer if you develop complications such as infections. Your risk of infection continues when going home and for the next few months (this will be longer if you have an allogeneic HCST), until your immune system returns to normal.

If you have received an allogeneic transplant, you may need to continue taking immunosuppressive drugs to reduce the risk of developing chronic GHVD.

What will happen on transplant day?

Your transplant will take place after you have finished your conditioning treatment (within one or two days).

You may be given medication to prevent any allergic reaction during the infusion of cells. Like a blood transfusion, you receive the stem cells intravenously through a central venous line possibly placed in your neck. The procedure takes between 30 minutes and an hour. You will be awake all the time and feel no pain. Your nurse will monitor your blood pressure and temperature during and after your transplant.

The infusion of stem cells is usually well tolerated, but in some cases, especially if the cells have been previously frozen, you may develop fever and chills, nausea and vomiting, dark urine and the perception of an unpleasant odour, which originates from the preservative used.

After entering the bloodstream, the stem cells travel through the circulation and reach your bone marrow, where, after two to three weeks, they begin to produce new blood cells.

If you have any questions or concerns about stem cell transplants, you can speak to one of our nurses or helpline volunteers on **08088 010 444**. The helpline is open weekdays 9:00am - 10:00pm and Saturdays 9:00am - 12:30pm.

Side effects

Because the conditioning treatment wipes out the cells in your bone marrow, the first month after the transplant you enter a phase of aplasia characterised by a decrease in the number of blood cells in your body (leukocytes, red blood cells and platelets), which can cause infections, haemorrhages and other complications.

Complications may derive from the intensity of the chemotherapy you are given or they may relate to the stem cell transplant. Many complications are common to all transplants but highly variable between patients. For this reason, it is not possible to anticipate the specific side effects that you might experience, or how intense they may be and for how long they will last. Your doctor will discuss with you potential side effects that may arise in your particular case.

After the transplant, you will be carefully monitored until your transplanted cells start to regenerate, a process where your bone marrow starts to produce enough blood cells to replace those that have been destroyed by the treatment. If you are in hospital during this time, you may receive visitors but they must be well and will need to wear protective clothing to protect you from getting an infection.

The length of your hospital stay depends on the type of transplant and conditioning treatment you have received, but usually lasts between two and four weeks after your transplant. You may be hospitalised for a longer period until your immune system recovers enough for you to go home, but some patients remain as outpatients during this time.

Side effects due to the conditioning (pre-transplant) chemotherapy

As expected, the higher the intensity of chemotherapy the more intense and lengthy the side effects. Below are some common early complications that you

may experience because of your conditioning treatment:

Nausea and vomiting

These are the most frequent complications after a stem cell transplant. Symptoms can start as soon as therapy is initiated and stop with the end of treatment. Current antiemetics (drugs to prevent nausea and vomiting) are very effective, and this side effect is usually tolerated relatively well.

Oral mucositis

This refers to the inflammation of the mucous membrane of the mouth. It usually appears five to seven days after the end of conditioning treatment, and disappears when the white blood cell counts return to normal levels. It can be painful and prevents an adequate food intake. If your ability for food intake is very limited, you may be given parenteral (intravenous) or enteral (by tube) nutrition.

Diarrhoea

This is a common side effect but easily managed with appropriate medication. It may start two to three days after initiating conditioning treatment, and usually lasts four to five days. To reduce the risk of infections, you need maximum hygiene of the anal area.

Parotitis

Inflammation of the parotid (mumps). It may happen if you have received total body irradiation. It usually appears after the first or second session of radiotherapy. The condition is easily countered with mild analgesics.

Hair loss (alopecia)

Hair loss does not constitute a clinical problem but an aesthetic problem, however, losing your hair may have a psychological impact. Hair loss occurs because the chemotherapy attacks the cells in your hair roots. Both men and women can be affected.

Chemotherapy may cause hair loss all over your body — not just on your scalp. Hair can fall out very quickly in clumps or gradually. Some chemotherapy drugs are more likely than others to cause hair loss, and different doses can cause anything from a mere thinning to complete baldness.

If you lose hair as a consequence of your treatment, it will usually grow again three to six months after your transplant, although it is not

Side effects (cont.)

uncommon that it changes some of its characteristics (more or less curly, more or less fatty, and more or less abundant).

No treatment exists that can guarantee your hair won't fall out during or after chemotherapy, but some treatments have been investigated to prevent hair loss.

For greater comfort and hygiene, you may opt for a good haircut (number 0, 1 or 2) before transplantation.

Infections, risk of bleeding and anaemia

Chemotherapy and immunosuppressant drugs weaken your immune system, making you vulnerable to infections. Immediately after having a transplant you may stay in a special, sterile room for the first few weeks. Your risk of infections will continue for the following months until your immune system recovers.

Depending on your risk of infection, several preventive measures may be taken. Over 90% of patients will have fever immediately after the transplant, and should be treated with antibiotics. Anaemia can cause you to feel tired, have palpitations, dizziness on sitting up and headache. To prevent anaemia you will receive as many red blood cell transfusions as necessary, in order to maintain your red blood cell counts within an acceptable level. The risk of bleeding is easily managed with platelet transfusions to keep your platelet counts above the level of haemorrhagic risk. Nowadays haemorrhagic complications are very uncommon.

Organ damage

The chemotherapy used for the transplant can harm your body's organs, such as the heart, lungs, kidneys, liver, bones and joints, and nervous system. Damage to your organs may also come from infections.

Infertility

The chemotherapy and radiotherapy given to treat your disease can cause infertility. In some cases, fertility is affected for a short period and recovers when the treatment has finished, but in

other cases fertility can be affected for longer.

Many people who are treated for cancer, particularly as children, do not experience infertility problems at all. It is difficult to determine who may be affected so it is worth discussing with your doctor before starting treatment.

If you are looking to start a family in the near future, then you may want to think about freezing your eggs or sperm before starting your treatment.

Serious unexpected side effects

After a stem cell transplant you are at risk of experiencing other less common but serious side effects, including:

Stem cell (graft) failure

This occurs when the donor stem cells fail to repopulate your bone marrow, or they do it for only a short period of time and is characterised by the inability to recover a normal number of leukocytes, platelets and red cells at 21-28 days after transplantation. It is an exceptional complication almost exclusively observed in 1) transplants from matched-unrelated donors (MUD) with incompatibilities in the HLA system; 2) transplants where T lymphocytes have been removed from the donor cells prior to the transplant; and 3) transplants with umbilical cord blood. This is an uncommon complication which may be overcome by infusion of additional stem cells. The stem cells used for this second transplant may be derived from either the same donor source or a different stem cell source. Graft failure can lead to serious complications.

Your doctors will be monitoring your blood cell counts regularly. This means if you do start to relapse you can get the best treatment straight away.

Blood in the urine

Bleeding in the urine caused by having chemotherapy and viral infections. It can be very displeasing, especially if you require a urinary catheter, and can

Side effects (cont.)

lead to lengthy hospitalisation.

Liver disease

The chemotherapy can cause the obstruction of the veins in your liver. It usually appears within the first 20 days of transplantation and in most cases it is resolved within a few days.

Complications in the lungs

Bleeding into the pulmonary alveoli (tiny air sacs in the lungs) is an exceptional but extremely serious complication that may appear during the first weeks after transplantation.

Other short term side effects include non-infectious pulmonary complications, such as idiopathic pneumonia, that may occur during the first two months post-transplant. It is more likely to happen in older patients or if you develop acute GVHD.

New cancers

Having a stem cell transplant increases your risk of developing a secondary malignancy. The main factors for developing secondary malignancies are the chemotherapy and radiotherapy given to treat your disease, certain infections and also genetic factors. Secondary malignancies are an extremely exceptional occurrence usually arising at least 10 years after the transplant.

Blood clots

Known as Thrombotic microangiopathy, the formation of a blood-clot as a result of blood-vessel damage induced by some drugs. This complication is usually exclusive of patients receiving an allogeneic transplant. Normally it does not produce symptoms, and it requires blood and platelet transfusions. It usually resolves with the modification of the treatment. In some cases the effect is caused by infections and GVHD, and is more difficult to control.

Side effects due to the stem cell transplant

A stem cell transplant carries several risks of complications, some potentially fatal. Some people experience minimal problems, but

others may develop complications that require treatment or hospitalisation.

The risk can depend on many factors, including your specific disease, type of transplant and chemotherapy, your age and your general state of health. When you have a stem cell transplant, it is not possible for your doctor to know in advance what specific complications you may suffer or their intensity.

Two to three weeks after your transplant, the stem cells will engraft in your bone marrow (this is called haematopoietic rescue or implant) and initiate a stable production of the different blood components (leukocytes, red blood cells and platelets). Your recovery is verified by a progressive increase in the number of leukocytes and platelets in your blood.

Complications associated with haematopoietic implant include:

- **Engraftment syndrome** - This term refers to the appearance of a series of signs and symptoms at around the time your neutrophils (a type of immune cell) are recovering. For this reason engraftment syndrome is thought to be caused by substances produced by immune cells, which cause leaking from blood vessels and organ dysfunction. Engraftment syndrome is characterised by the appearance of high non-infectious fever. The fever is usually associated to a rash, an incorrect oxygenation of the blood in the lungs and diarrhoea. Sometimes the syndrome can be confused for GVHD. Engraftment syndrome is a mild complication and, if properly diagnosed and treated, resolves within a few days.
- **Cytomegalovirus (CMV) disease** - CMV is a common virus that can infect anyone. Once infected, the virus remains latent ('sleeping') for life in peripheral blood leukocytes. In most people, this causes no symptoms and treatment is not required. Under certain conditions, such as when your immune system is low,

Side effects (cont.)

the virus can be re-activated. If you are CMV-positive before your transplant, the virus can re-activate after the transplant because your immune system is weakened from the chemotherapy and immunosuppressant drugs.

- **Cataracts** - This is a clouding of the lens of the eye, which causes vision loss. Cataracts may appear at five to six years after transplantation if you have received total body irradiation. It is advisable that after a transplant you have annual ophthalmologic examination. Cataracts are easily resolved with surgery.

Another common complication of stem cell transplantation is graft-versus-host disease (GVHD). This is given special consideration in the next section.

Graft-versus-host disease

GVHD is a complication that can only develop if you have an allogeneic stem cell transplant. GVHD occurs when the cells from the donor attack your organs and tissues.

It is important to consider that whilst GVHD can impact your quality of life, it does have some benefit. The same immune response responsible for attacking your normal cells also targets and destroys any surviving cancer cells. This is called the graft-versus-leukaemia (GVL) or graft-versus-tumour effect. Patients who develop GVHD have lower disease relapse rates.

There are two forms of GVHD:

1. Acute GVHD
2. Chronic GVHD

The acute form usually appears during the first three months after your transplant, whereas the chronic form may appear at a later stage.

The immune system is the tool your body uses to fight infections, and also to recognise self and non-self through the unique HLA signature expressed on the surface of your cells. When you first receive cells from a donor, these cells do not recognise the HLA signature on your own cells. They will consider your body as something foreign and will therefore react and attack your organs and tissues, causing GVHD.

The more the HLA mismatch between you and your donor, the greater the risk of developing GVHD. This may occur even though you and your donor are fully compatible, since there are always differences in the HLA signature between two individuals; the only exception being allogeneic transplants between identical twins (syngeneic transplantation).

To lower the risk of GVHD, you may be given immunosuppressive medication a few days before your transplant, and continue taking the medication for a few months after. Some of these drugs include ciclosporine or a combination of mycophenolate mofetil (MMF) and tacrolimus. After the transplant

Graft-versus-host disease (cont.)

you can also receive another immunosuppressive drug called cyclophosphamide, usually starting three to five days after the transplant. The risk of GVHD can also be reduced by removing the T lymphocytes from your donor's bone marrow or peripheral blood, after it has been donated. New therapies are constantly being tried out, and your doctor can explain what the best option may be for you.

Acute GVHD

Acute GVHD can mainly affect your skin, gut and liver. To confirm the diagnosis a tissue biopsy may be required. Depending on the number and severity of organs affected, GVHD is graded one to four. Grade one represents a mild form of GVHD and may not require treatment and grade four represents the most severe form.

Your symptoms will reflect which organ(s) are affected, and most commonly will manifest as:

- **Skin lesions, consistent with a rash resembling that of measles** - It can affect your whole body and, exceptionally, evolve to blisters and vesicles similar to those of a burn.
- **Sickness and diarrhoea, resulting from bowel involvement** - You may be given antiemetics to treat your sickness and painkillers if you have abdominal cramps. To avoid dehydration you may be given fluids by drip into a vein. If you can't eat and are losing weight you may be fed through a tube running from the nose to the stomach (nasogastric tube).
- **Jaundice** - Yellowing of your eyes and skin as a manifestation of liver involvement. Your skin may be itchy and this can be managed with medication. If required, you will have blood transfusions to recover your normal red blood cells and platelet numbers.

Chronic GVHD

It may occur as a complication later after your transplant; sometimes years later, whether you have had the acute form or not. Chronic GVHD might occur in the skin, liver, eyes,

mouth, lungs, gut, neuromuscular system, or genitourinary tract.

The most common symptoms of chronic GVHD include:

- **Skin lesions** - For example scleroderma, characterised by a hardening of your skin.
- **Abdominal swelling and jaundice, when your liver is affected.**
- **Sjögren's syndrome (dry eye syndrome)** - This consists of dry mouth and/or grit sensation in your eyes. These manifestations are usually very annoying and require you taking extreme care to avoid lesions and infections in the oral mucosa or cornea. You may need intensive treatment if the syndrome manifests in its most serious form. Dry eye syndrome may be associated with vaginal dryness, which should be treated by a gynaecologist.
- **Difficulty swallowing, pain with swallowing and weight loss** - You might find it uncomfortable in your throat when swallowing. This might impact on your appetite and decrease your food intake, meaning that weight loss might be expected.
- **Problems with urinating** - Increased need to urinate and a sensation of burning or bleeding with urination, indicative of the genitourinary system being affected.

If you develop chronic GVHD you may be given long-term immunosuppressive drugs. These drugs can compromise your immune system and therefore you will have a higher risk of infections. Your doctor may prescribe medicines to help prevent infections.

What will happen if I go back into hospital after a stem cell transplant?

Once discharged, you may need to return to hospital for the treatment of some complication. The more frequent causes for rehospitalisation are insufficient fluid intake, infections and GVHD. Hospital readmissions in the first three to six months after transplantation are frequent and, for the most part, easily resolved.

You must contact your medical team immediately if you have any of the following symptoms:

- A high temperature of 38°C (100.4 F) or above
- Shivering
- Breathing difficulties
- Chest pain
- Flu-like symptoms – such as muscle aches and pain
- Bleeding gums or nose
- Bleeding from another part of the body that doesn't stop after applying pressure for 10 minutes
- Mouth ulcers that stop you eating or drinking
- Vomiting that continues despite taking anti-sickness medication
- Four or more bouts of diarrhoea in a day
- New or worsening skin rash

You will also need to go back to hospital for regular checks. Hospital visits will be more frequent at the beginning but more spaced out as your health improves. In these visits, you will have blood tests, a physical examination and your medication will be reviewed. Complementary tests may include a bone marrow biopsy and a scan to check the state of your organs. In the long-term you may need to visit the hospital once or twice a year.

When you receive a Haematopoietic stem cell transplant you are effectively receiving a new immune system. The cells that constitute this complex system, the lymphocytes, develop from the stem cells transplanted. For lymphocytes to become effective in defending your organism, they need a period during which

they increase their numbers and "learn" to recognise the enemy (the infectious agents) and keep an "immunological memory." From an immunological point of view, after a transplant your immune system behaves like that of a newborn. For this reason, you must be revaccinated. You will start vaccination approximately 12 months after your transplant. In patients with active GVHD, with corticosteroid treatment or with several immunosuppressants, vaccination may be delayed. Compulsory vaccines are those for pneumococcus, hepatitis A + B, Haemophilus influenzae, diphtheria, tetanus, pertussis, polio Salk, measles, rubella and parotitis.

What happens if my transplant doesn't work?

Your transplant may not work because the cells from your donor are not accepted by your body (graft rejection or graft failure) or because your original condition comes back after some time (relapse).

Graft rejection is not very common but it can happen at any time for the next two years after your transplant, as this is the time it may take for your immune system to recover fully. During this period, you may need donor lymphocyte infusions. Your medical team will monitor you closely for signs of graft rejection. If graft rejection is confirmed, you may need another stem cell transplant.

Unfortunately, transplantation does not always ensure the eradication of your illness. The chance of the disease coming back varies depending on your disease and the type of transplant you have had. Relapses are more likely to happen in the first two years after transplantation, and are less common after five years. You will have regular checks to assure that your disease is not returning.

There are a number of treatment options at relapse depending on the type of disease, your state of fitness, your original response to the chemotherapy and the time from transplantation to relapse.

There isn't a general rule to treat relapse, so if your disease comes back after a transplant you should discuss with your medical team the different options available. If you relapse after having an allogeneic transplant, one possibility is to have additional chemotherapy and an infusion of donor T lymphocytes, to try and enhance the anti-tumour effect.

Some patients may not be able to have further treatment because of the high risk; and sometimes patients may decide not to continue their treatment. In these cases, you may have palliative care. Palliative care may involve transfusions, antibiotics and medication to help you deal with the symptoms of the disease. You and your family will receive advice and support from your medical team at all stages.

Glossary

Aplasia

A haematologic disorder in which the normal progression of cell generation and development does not occur.

Allogeneic stem cell transplantation

A transplant modality in which donor and recipient are different persons.

Autologous stem cell transplantation

A transplant modality in which donor and recipient are the same person.

Bone marrow

The soft tissue located inside some bones, where blood cells generate.

Bone marrow registry

The institution responsible for keeping a list of bone marrow donors and their characteristics.

Bone marrow transplant

The process of transferring bone marrow cells from donor to recipient.

Chemotherapy

A combination of one or more drugs to treat cancer.

Conditioning treatment

A treatment with high-dose chemotherapy and/or radiation therapy given to prepare your body for a stem cell transplant. Depending on the intensity of the treatment there are three main types of conditioning: myeloablataive, reduced intensity (RIC) and non-myeloablative.

Cord blood bank

An institution, public or private, responsible for storing donor cord blood stem cells for transplantation purposes.

Cord blood transplant

A modality of allogeneic transplantation where stem cells

Glossary (cont.)

collected from the umbilical cord are transferred on to a patient.

Cord blood unit

An item of cord blood stem cells from a single donation that has been cryopreserved and stored in a cord blood bank for transplantation purposes.

Cytomegalovirus (CMV)

A virus of the herpes family that can be re-activated in immunosuppressed patients who already had the virus before their transplant, or can be transferred when present in the cells from the donor. CMV infections can cause serious complications in transplant patients.

Engraftment

The correct implantation of transplanted cells in the recipient.

Engraftment syndrome

A potential early complication around the time of neutrophil recovery after stem cell transplantation. Symptoms resemble those of GVHD.

Graft

Living tissue that is transplanted surgically.

Graft failure (stem cell failure)

A complication following a stem cell transplant where the cells of the donor fail to implant (engraft) in the recipient.

Graft-versus-host disease (GVHD)

A detrimental effect of allogeneic transplantation when the T lymphocytes of the donor attack the healthy tissues and organs of the patient. GVHD can be acute or chronic.

Graft-versus-leukaemia (GVL)

A beneficial effect of allogeneic transplantation when the T lymphocytes from the donor attack and kill the neoplastic cells of the patient.

Haematopoiesis

The biological process of blood

cell formation.

Haematopoietic rescue

The process of recovering the bone marrow function after high-dose chemotherapy, by transplanting haematopietic stem cells.

Haematopoietic stem cells

Specialised cells responsible for producing all other blood cells.

Haploidentical transplants

A modality of allogeneic transplantation where the donor is a relative of the patient but their HLA identity is not ideal for transplantation purposes.

HLA identity (or compatibility)

The degree of similarity between the HLA antigens of donor and patient.

Human Leukocyte Antigen (HLA) antigens

A unique protein signature expressed on the surface of most cells in the body of every person.

Immunosuppressive drugs (immunosuppressant)

A class of drugs that reduce the strength of the immune system.

Leukocytes (white blood cells)

Immune cells responsible for fighting infection. These include T and B lymphocytes, granulocytes and monocytes.

Lymphocytes

A subtype of leukocyte (white blood cell). Includes T and B lymphocytes (T and B cells) and natural killer cells.

Matched Unrelated Donor (MUD) transplant

A modality of allogeneic transplantation where the donor is not related to the patient but shares an acceptable HLA identity for transplantation purposes.

Myeloablation

Condition in which bone marrow activity is decreased, resulting in fewer red blood cells, white blood

Glossary (cont.)

cells, and platelets. It is a side effect of some cancer treatments.

Peripheral blood stem cells (PBSC)

Circulating haematopoietic stem cells.

Peripheral blood stem cells (PBSC) transplant

The process of transferring circulating haematopoietic stem cells from donor to recipient.

Platelets

Circulating cells responsible for forming blood clots.

Radiotherapy

A therapy that uses ionizing radiation, generally as part of cancer treatment.

Red blood cells

Circulating cells responsible for carrying oxygen.

Relapse

The return of the disease after a period of remission.

Secondary malignancies

New cancers arising from the chemotherapy used for treating a disease.

Stem cell transplant

The process of transferring haematopoietic stem cells from donor to recipient.

Sjögren's syndrome (dry eye syndrome)

May be caused by GVHD and consists of dry mouth and/or grit sensation in the eyes.

Syngeneic transplant

A modality of stem cell transplantation where donor and recipient are identical twins.

Tandem transplantation

A modality of stem cell transplantation where patients receive two consecutive stem cell transplants spaced a few weeks or months apart.

Useful contacts and further support

There are a number of helpful sources to support you during your diagnosis, treatment and beyond, including:

- Your haematologist and healthcare team
- Your family and friends
- Your psychologist (ask your haematologist or CNS for a referral)
- Reliable online sources, such as Leukaemia Care
- Charitable organisations

There are a number of organisations, including ourselves, who provide expert advice and information.

Leukaemia Care

We are a charity dedicated to supporting anyone affected by the diagnosis of any blood cancer. We provide emotional support through a range of support services including a helpline, patient and carer conferences, support group, informative website, one-to-one buddy service and high-quality patient information. We also have a nurse on our help line for any medical queries relating to your diagnosis.

Helpline: **08088 010 444**
www.leukaemiacare.org.uk
care@leukaemiacare.org.uk

Bloodwise

Bloodwise is the leading charity into the research of blood cancers. They offer support to patients, their family and friends through patient services.

020 7504 2200
www.bloodwise.org.uk

Cancer Research UK

Cancer Research UK is a leading charity dedicated to cancer research.

0808 800 4040
www.cancerresearchuk.org

Macmillan

Macmillan provides free practical, medical and financial support for people facing cancer.

0808 808 0000
www.macmillan.org.uk

Maggie's Centres

Maggie's offers free practical, emotional and social support to people with cancer and their families and friends.

0300 123 1801
www.maggiescentres.org

Citizens Advice Bureau (CAB)

Offers advice on benefits and financial assistance.

08444 111 444
www.adviceguide.org.uk

Leukaemia Care is a national charity dedicated to providing information, advice and support to anyone affected by a blood cancer.

Around 34,000 new cases of blood cancer are diagnosed in the UK each year. We are here to support you, whether you're a patient, carer or family member.

Want to talk?

Helpline: **08088 010 444**
(free from landlines and all major mobile networks)

Office Line: **01905 755977**

www.leukaemiacare.org.uk

care@leukaemiacare.org.uk

Leukaemia Care,
One Birch Court,
Blackpole East,
Worcester,
WR3 8SG

Registered charity
259483 and SC039207

Leukaemia Care
YOUR Blood Cancer Charity

Health & care information you can trust
The Information Standard Certified Member