Allogeneic Stem Cell Transplants

A Guide for Patients

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

A stem cell transplant is a procedure to provide patients with healthy bone marrow cells when their own are either not working correctly or have been depleted by intensive chemotherapy treatment.

The booklet was written by Dr Oscar Berlanga and updated by our Patient Information Writer, Isabelle Leach. It has been reviewed by Christine Lim, Post-Bone Marrow Transplant Clinical Nurse Specialist at King's College Hospital, our Nurse Advisor Fiona Heath and Jonathan Kay, Patient Information Writer and Researcher at Anthony Nolan.

Thank you to our patient reviewers John Watson and Paul Cabban for providing valuable feedback.

If you need specific advice or are concerned about anything regarding stem cell transplants, please contact your medical team or clinical nurse specialist.

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 8:30am – 5:00pm Monday - Friday and 7:00pm – 10:00pm on Thursdays and Fridays. If you need someone to talk to, call **08088 010 444**.

Alternatively, you can send a message via WhatsApp on **07500068065** on weekdays 9:00am – 5:00pm.

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** or over the phone on **08088 010 444**.

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/support-and-information/help-and-resources/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/support-and-information/support-for-you/find-a-support-group/**

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 **support@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**.

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 magazine includes inspirational patient and carer stories as well as informative articles by medical professionals: **www.leukaemiacare.org.uk/communication-preferences/**

What are stem cells?

Stem cells are the base cells in the body that have the ability to develop into any of the body's specialised cells. Stem cells in your bone marrow, the soft tissue inside the bones, are known as haematopoietic stem cells.

Haematopoietic stem cells can develop and mature to become any of three types of blood cell:

- White blood cells, which fight infection
- Red blood cells, which carry oxygen
- Platelets, which help the blood to clot

The development and maturation of stem cells is known as haematopoiesis.

As well as being able to develop into any blood cell required, stem cells also have the capacity to self-replicate into identical copies. This means stem cells will be present throughout life to ensure a constant supply of blood cells.

Every day, stem cells produce billions of new blood cells. If stem cells are damaged and unable to perform this function, medical intervention will be required promptly.

Stem cells are found in the bone marrow, peripheral blood (blood circulating in the body and not present in organs) and the umbilical cord. Cells from any of these sources can be used for transplants.

What is a stem cell transplant?

A stem cell transplant (SCT) is a procedure to provide patients with healthy bone marrow cells when their own are damaged or have been destroyed by chemotherapy treatment.

The most common reason for a SCT is when a patient has a cancer that can only be cured with high doses of chemotherapy. The chemotherapy destroys the cancer cells but also damages the patient's stem cells in the bone marrow. Following the chemotherapy, stem cells are transplanted to restore the bone marrow.

Stem cells can be transplanted from the same individual (autologous SCT) or a donor (allogeneic SCT).

Autologous SCT (auto-SCT)

The transplanted stem cells are from the same person who is receiving the transplant. Before the patient receives treatment with high doses of chemotherapy, the stem cells are collected, stored and frozen.

After chemotherapy treatment, the stem cells are returned to the patient via an intravenous drip infusion. The stem cells then travel to the bone marrow and start making new blood cells.

Allogeneic SCT (allo-SCT)

Stem cells come from a matching donor, sometimes a family member, or a closely matched unrelated donor. After the chemotherapy treatment, the stem cells are transplanted and travel to the bone marrow where they begin to produce new blood cells. The transplant restores the supply of normal cells that have been destroyed by the intensive chemotherapy, but also, the transplanted donor's T-lymphocyte cells (T-cells) recognise and destroy any leukaemia cells that were not eliminated by the chemotherapy and so substantially reduce the risk of relapse. This is known as the graft versus leukaemia (GVL) effect.

Who receives a stem cell transplant?

SCTs have the potential to treat patients with a number of conditions including leukaemia, myeloma, lymphoma, myelodysplastic syndromes and congenital blood conditions such as thalassaemia or sickle cell disease. SCTs are also used successfully for autoimmune diseases such as systemic lupus erythematosus, multiple sclerosis and rheumatoid arthritis.

The type of transplant which is selected for you by your haematologist (autologous or allogeneic) will depend on your age, state of health, the stage and status of your leukaemia, the possibility of collecting disease-free stem cells and the availability of a suitable donor.

Allo-SCTs are usually given to young fit patients because of their ability to withstand the intensive chemotherapy, and the greater likelihood of complications with allo-SCTs that occur in older patients. However, depending on their health and fitness, reduced intensity transplants may be an option for older patients.

Allo-SCTs are the obvious choice for patients whose bone marrow cannot generate their own blood cells such as in aplastic anaemia, since allo-SCTs use stem cells from a healthy donor.

Auto-SCTs do not require finding a matched donor. Patients who have an auto-SCT rarely have a graft failure since the patient is receiving their own cells, and they have a lower risk of infections. Grafting of the patient's own stem cells occurs more quickly than with donor cells.

Both allo-SCTs and auto-SCTs can be used in patients with lymphoma or multiple myeloma according to the patient's clinical requirements.

For patients with leukaemia such as acute myeloid leukaemia, acute lymphoblastic leukaemia and plasma cell leukaemia, both types of SCT can be used depending on which is best for the patient.

In patients with chronic myeloid leukaemia, an allo-SCT following a tyrosine kinase inhibitor

is the usual treatment. For chronic lymphocytic leukaemia, chemotherapy, immunotherapy and/or targeted therapy can achieve a reduction in the number of leukaemia cells, keeping symptoms under control. However, if required, SCTs allow the use of high doses of chemotherapy. Since an auto-SCT uses the patient's own stem cells which may include leukaemia cells, allo-SCTs are more commonly used.

This 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 Patient Services team at **08088 010 444** or email **support@leukaemiacare.org.uk**

Donors for allogeneic stem cell transplants

The outcome of an allo-SCT depends on finding a matching donor. The closer the match of the donor to the recipient, the more likely the transplant will be successful. Siblings are often compatible donors.

In general, if you have more than one donor (family or non-relative) that are a full match the following criteria are preferred:

- Younger donors
- Male donors regardless of the recipient's sex
- Similar weight as the recipient
- A matched cytomegalovirus status

Sibling donors

The ideal donor is a sibling with an identical Human Leukocyte Antigen (HLA) match. HLA proteins are located on the surface of most cells in your body and they are the main way the immune system tells the difference between your own cells and foreign cells. The degree of HLA matching between you and your donor is the single most significant factor contributing to a successful transplant.

When you have an HLA tissue typing test, both you and your potential donor must provide a blood or saliva sample. The samples are analysed and compared in the laboratory to identify if you have enough HLAs in common.

Patients have a 25% chance of a sibling being a full HLA match, because siblings inherit 50% of HLA antigens from each parent.

However, if your sibling is an identical twin where one fertilised egg has divided, the donor is genetically identical and is called a syngeneic donor. In this case there will be no GVL, rejection of the graft or graft-versus-host disease (GVHD), which occurs when the T-cells from your donor attack your organs and tissues.

For non-identical twins where two separate eggs have developed at the same time in the uterus, the chance of being fully HLA matched is the same as for a normal

sibling.

Unfortunately, only 30% of patients have an HLA-matched sibling, which means the option for a donor for the remaining 70% patients will be a matched unrelated donor, a haploidentical donor or a cord blood unit.

Matched unrelated donors

In many cases, donor registries are used to find the appropriate match using tissue typing. The requirement to be a match may be 10 out of 10 HLA antigens (10/10) or, more recently, 12 out of 12 HLA antigens (12/12).

Dependent on their ethnicity, up to 5% of patients will not be able to find a match in the Bone Marrow Donor Worldwide database. Patients in Europe requiring an allo-SCT have a 45% to 65% chance of finding a 10/10 matched donor, and a 20% to 30% chance of locating a 9/10 matched donor.

Haploidentical donors

For patients who do not have a closely matched unrelated donor, options include a haploidentical donor, a cord blood unit or a mismatched unrelated donor.

A haploidentical donor is a family member with a 50% HLA. Using an haploidentical donor increases the possibility of finding a donor as most people have at least one haploidentical relative.

Moreover, it is easier and quicker to request a relative to donate stem cells.

While using a haploidentical donor can be complicated because of the high risk of rejection or severe GVHD, new methods have been developed to overcome this risk by eliminating the donor T-cells responsible for GVHD prior to the transplant, and by improving the treatments available for GVHD.

Cord blood donors

As with bone marrow and peripheral blood, umbilical cord blood can be a source of stem cells for allo-SCTs. Blood-forming stem cells are available from the cord and placenta after a baby is

Donors for allogeneic stem cell transplants (cont.)

born. Donated cord blood is frozen and stored at a cord blood bank for future use. The NHS Cord Blood Bank, which was set up in 1996, collects, processes and stores cord blood for the public. Anthony Nolan also collect and store cord blood. There is no charge to the donor.

Since the umbilical cord stem cells are relatively immature, the HLA matching is less important compared with using stem cells from bone marrow or peripheral blood. For cord blood transplants, cord blood with the maximum possible number of stem cells is the main criteria.

With umbilical cord stem cells, there is a reduced potential for transmission of viruses from the donor, and the relative immaturity of the immune cells reduces the chances of experiencing GVHD. Moreover, because it is already stored in a cord blood bank, the process is quicker than with haploidentical donors where family members need to be willing to donate.

Stem cell transplant procedure

Assuming you have a well-matched donor, there are five main stages to be completed in an allo-SCT procedure.

Your healthcare team will discuss with you the different stages involved and the effects that the transplant might have on you. The procedure is both physically and emotionally demanding. The first stage will be to assess your level of fitness and suitability for the transplant.

Stage 1: Your assessment for the transplant

Your medical team will assess your general health and if it is appropriate for you to receive donor stem cells. They will perform the following tests to ensure this:

Blood tests

These will indicate if your blood cell counts are normal and assess your liver and kidney function. Blood tests will also identify if you have had any previous exposure to infectious diseases such as hepatitis, cytomegalovirus (CMV) and human immunodeficiency virus (HIV). These may possibly be reactivated when your immune system is weakened.

Electrocardiogram and 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 the structures of your heart and how well your heart is working. These tests will check the rhythm and electrical activity of your heart and ensure your heart and nearby blood vessels are normal.

X-rays and/or computerised tomography (CT) scans

These imaging techniques will check the condition of your organs such as the lungs, liver and kidneys.

Dental check-up

Any tooth decay can potentially be a source of infection during your transplant so it is important to have them checked.

Other tests

You may also have other tests that your doctor considers necessary. These may include pulmonary function tests to see how well your lungs are working and specific liver or kidney function tests.

You will also have an up-to-date bone marrow biopsy, if necessary, to see if your bone marrow is ready for the transplant.

A number of patients will also have a central (Hickman) line inserted into a vein in the chest, sometimes with several tubes (or heads), to allow for chemotherapy drugs and other treatments to be administered at the same time.

Stage 2: Collecting the stem cells

The stem cells must be collected from the donor during this stage. Bone marrow transplants require removing the stem cells from the donor's bone marrow under a general anaesthetic. The bone marrow is the main source of blood stem cells, however, with the use of special drugs they can be moved out of the bone marrow into the blood where they are easier to collect and an anaesthetic is not required for this process.

The majority of transplants now use stem cells from peripheral blood. Stem cells can also be collected from umbilical cord blood.

Collecting stem cells from blood

This involves separating the stem cells out of the blood. To boost the number of stem cells in the blood, the donor is given a subcutaneous injection of a drug called a Granulocyte Colony Stimulating Factor (GCSF) for a few days 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, a 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

Stem cell transplant procedure (cont.)

body through the other arm. This procedure, known as apheresis, 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 and syringe. One needle is inserted usually on each side of the hip, to ensure enough bone marrow is collected. 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. After the bone marrow is obtained, it is filtered and stored in specialised bags before being frozen. When required, the bone marrow solution is defrosted and given to the patient through a vein.

Collecting stem cells from umbilical cord blood

Stem cells can be collected from the cord and placenta after a baby is born. Donated cord blood is frozen and stored at a cord blood bank for future use. Cord blood transplants are easy and safe. Moreover, because they are already stored in a cord blood bank, the stem cells are readily available.

Stage 3: Conditioning treatment

Conditioning treatment is the name given to the chemotherapy regimen, which can be given with or without radiotherapy, to eliminate the leukaemia cells and prepare your bone marrow for receiving the stem cells. It is generally given during the week before your transplant. Conditioning treatment may last up to a week and you may need to remain in hospital while receiving the treatment.

The chemotherapy is administered intravenously through a central venous line,

which is a thin tube inserted into a large vein near your heart through your chest wall. This central line stays in place throughout your treatment, which makes it easier for your medical team to administer drugs.

The type of conditioning chemotherapy you receive will be determined by your medical team based on your type of disease, age and general health. Depending on their intensity, conditioning regimens are classified as:

- **Full intensity or myeloablative:** Conditioning which kills all your bone marrow cells as well as the leukaemia cells.
- **Reduced-intensity:** Conditioning which kills the leukaemia cells and only some of your bone marrow cells.
- **Non-myeloablative:** Conditioning which does not kill all of the leukaemia cells and very few of your bone marrow cells.

Your doctor will discuss with you the best option for your particular case.

Full intensity (myeloablative) conditioning

This was the first type of conditioning treatment developed for bone marrow transplants. Myeloablative conditioning is used for:

- Removing the leukaemia cells from your body
- Creating space in your bone marrow for the new stem cells
- Avoiding your immune system rejecting the transplanted cells

Because myeloablative conditioning is so strong, it removes all your existing blood stem cells, so you need a stem cell transplant to recover your ability to generate new blood cells.

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

Stem cell transplant procedure (cont.)

Reduced intensity conditioning

Reduced intensity conditioning is an alternative for patients who are not able to withstand full intensity conditioning treatment. It involves a combination of chemotherapy and immunosuppressive agents. Chemotherapeutic agents target and eliminate the leukaemia cells. Unlike myeloablative conditioning, the dose of chemotherapy in reduced intensity conditioning is high enough to kill some but not all of the cells in your bone marrow. You are also given immunosuppressive therapy to lessen the activity of your own immune system and prevent it from attacking the cells from the donor when infused.

With reduced intensity conditioning, your cells and the cells from the donor are present together in your bone marrow for a certain period of time, until the cells of the donor gradually and completely replace your own. During this process, the leukaemia cells are also destroyed by the donor's T-cells.

Unfortunately, after a transplant with reduced intensity conditioning, there is a higher chance of developing complications or a relapse.

Non-myeloablative conditioning

Non-myeloablative conditioning regimens are designed just to suppress your immune system sufficiently to allow the donor cells to get established in your bone marrow.

Low doses of chemotherapy and/or radiotherapy are used to decrease the toxicity of the regimen for more vulnerable patients. Therefore, the non-myeloablative conditioning is not strong enough to kill all of the leukaemia cells and only kills a small number of your bone marrow cells. It relies on the GVL effect where the donor T-cells recognise and destroy the leukaemia cells that were not eliminated by the chemotherapy and so substantially reduce the risk of relapse.

Because the non-myeloablative conditioning does not destroy your bone marrow stem cells, it is usually followed by an immunosuppressant to decrease the risk of rejection of the donated cells.

Non-myeloablative conditioning regimens represent a practical option for older patients and those with other illnesses who cannot be treated with myeloablative conditioning.

Stage 4: Infusion of the donor cells

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 the chemotherapy, 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 20 of this booklet.

Stage 5: Engraftment and recovery

After the transplant, you may need to stay in hospital for several weeks, until the infused stem cells engraft in your bone marrow and start producing new blood cells. Engraft is the medical term used for the grafting of the stem cells in your bone marrow.

During this period, you can experience a number of side effects such as tiredness, vomiting, diarrhoea and loss of appetite. It is also important to try and prevent infections as much as possible. You are likely to stay in a room by yourself in the hospital because of the increased risk of infection. Visitors will 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 have daily blood tests and regular temperature checks.

Depending on your health and your test results after the transplant, you may be able to recover as an outpatient, but you will still need full-time care by someone who can fulfil your medical and physical needs and take you to daily hospital visits.

You will usually leave hospital one or two months after the transplant, but may need to stay longer if you develop complications such as infections. Your risk of infection continues when you go home and for the next few months, until your immune system returns to normal.

What will happen on transplant day?

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

You may be given medication to prevent any allergic reaction during the infusion of cells.

Like a blood transfusion, you will receive the stem cells intravenously through a central venous line. 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, 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 a member of our Patient Advocacy team on **08088 010 444.**

Side effects

Because the conditioning treatment destroys the cells in your bone marrow in the first month after the transplant, the number of blood cells in your body are dramatically reduced, which can lead to infections, bleeding and other complications.

Many complications are common to all transplants but they can be 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 engraft and your bone marrow starts to produce enough blood cells to replace those that have been destroyed by the conditioning treatment.

Side effects or complications may be due to the intensity of the conditioning chemotherapy you are given or they may relate to the stem cell transplant itself.

Side effects due to conditioning chemotherapy

As might be expected, the higher the intensity of the chemotherapy, the greater number of side effects that you may experience. Below are some common side effects that you may go through because of your conditioning treatment, as well as some suggested coping strategies:

Nausea and vomiting

These are the most frequent side effects after conditioning for a SCT. Symptoms can appear as soon as therapy has started and stop with the end of treatment. Current anti-emetics (drugs to prevent nausea and vomiting) are very effective, and these side effects are usually relatively well tolerated.

Aside from medication, there are several things that might help with your nausea and/or vomiting:

- If the smell or preparation of food is putting you off eating or making you feel sick, then getting someone else to cook may prevent this.
- Ginger flavoured things (such

Side effects (cont.)

as juice or biscuits) can help with nausea.

- Stick to simple, fresh meals and try to avoid fried, highly flavoured foods.
- You might find it easier to eat smaller meals, more often than larger meals over longer periods of time.

Oral mucositis

This is inflammation of the mucous membrane in the mouth. It usually appears five to seven days after the end of conditioning treatment, and disappears when your white blood cells return to their normal levels. It can be painful and prevent you from eating properly, but sucking on ice cubes or using certain mouthwashes can provide some relief. If it continues to prevent you from eating sufficiently, you may be given liquid nutrition intravenously or via a nasogastric tube.

Diarrhoea

This is a common side effect but it is easily managed with appropriate medication, regular meals following a balanced diet and walking to help regulate the bowels. It may start two to three days after initiating conditioning treatment, and usually lasts four to five days. To prevent the risk of infections, you need to observe the best possible hygiene of the anal area.

Parotitis

This is inflammation of the parotid gland which is situated in front of the ears on each side of the face, and is responsible for producing saliva. Parotitis may happen if you have received total body irradiation. It usually appears after the first or second session of radiotherapy. The condition is easily treated with mild analgesics.

Hair loss (alopecia)

Hair loss does not constitute a clinical problem, but can 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. Hair can fall out very quickly in clumps or gradually. Some chemotherapy drugs are more likely to cause hair loss than others, and

different doses of the same drugs can cause anything from a mere thinning to complete baldness.

If you lose hair as a consequence of your treatment, it will usually grow back three to six months after your transplant, although it is not uncommon for your hair to change some of its characteristics in terms of texture, colour or quantity.

To help cope with the loss of your hair, there are a number of options:

- Wigs (some can be provided for free by the NHS to inpatients)
- Head scarves
- Hats
- A very short haircut (which can also be for greater comfort and hygiene)

Infections

Chemotherapy and immunosuppressant drugs weaken your immune system, making you vulnerable to infections. Despite the precautions to prevent infections taken straight after your transplant, you must remain aware that your risk of infection will continue in 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 they should be treated with antibiotics.

There are a number of things you can do to help you avoid infection:

- Follow a neutropenic diet using well-cooked and fresh products
- Minimise contact with those who may have infections, especially in crowds
- Try to maintain a good level of hygiene

Anaemia and risk of bleeding

Anaemia, which is a low level of red blood cells, 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.

The risk of bleeding occurs because you may have low levels of platelets, which are small blood cells that help the body form clots to stop bleeding. This is easily managed with platelet

Side effects (cont.)

transfusions to keep your platelet counts above the level where bleeding may be a risk. Nowadays bleeding complications are very uncommon.

Organ damage

The chemotherapy used in the conditioning regimen may 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 you can cause infertility. In some cases, fertility is affected only for a short period and recovers when the treatment has finished, but in other cases, fertility can be affected for longer.

Many patients, particularly children, do not experience any infertility problems. It is difficult to determine who may be affected, so it is worth discussing it 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.

Haemorrhagic cystitis

This is a serious inflammation of the bladder lining characterised by pain and difficulty in urinating, blood in the urine or haemorrhaging from the blood vessels that supply the inside of your bladder.

It often arises from chemotherapy or radiotherapy treatment, but can also be caused by viral or bacterial infections. It can be very distressing, especially if you require a urinary catheter, and it may lead to lengthy hospitalisation.

Liver veno-occlusive disease

This is the obstruction of the veins in your liver which is generally caused by the chemotherapy in the conditioning regimen. It usually appears within the first 20 days of the transplant and the symptoms include abdominal pain and swelling, weight gain and jaundice. If severe, it can be life-threatening. In patients with mild veno-occlusive disease, the condition resolves by itself and no treatment is required. For patients with moderate and

severe veno-occlusive disease, the aim of treatment is to provide supportive care with diuretics, oxygen, anticoagulants and haemodialysis.

Lung complications

Pneumonitis, which is non-infectious inflammation of the lung, or pneumonia, which may require antibiotics, are short-term complications that can develop within a couple of months of the transplant.

Diffuse alveolar haemorrhage, which is bleeding into the pulmonary alveoli (tiny air sacs in the lungs), is a serious complication that can occur in the first couple of weeks after the transplant, but fortunately it is very rare.

Thrombotic microangiopathy

This is the formation of blood clots in the small blood vessels throughout the body as a result of injury to the lining of the blood vessels. This can occur after a SCT, when the damage to the blood vessels is invariably due to the drugs used in the conditioning regimen. Normally it does not produce symptoms, but it does require blood and platelet transfusions. It usually resolves with the modification of the treatment. In some cases, the effect is caused by infections, and is more difficult to control.

Secondary cancers

Having a stem cell transplant increases your risk of developing a secondary cancer which may be unrelated to the leukaemia you had the SCT for:

- Blood cancers usually arise at three to seven years after your SCT
- Solid tumours can occur up to 15 years after the transplant
- The sensitivity of your skin can be increased, which can lead to a risk of developing skin cancer. However, this risk can be minimised by keeping out of the sun and using high-factor sun creams.

The incidence of secondary cancers is relatively low at around 5% of patients after 10 years of follow-up.

The reasons for developing these secondary cancers are poorly understood, but it is thought

Side effects (cont.)

that the transplantation process itself or the conditioning regimen, particularly the high dose regimens, may be involved.

Side effects due to the stem cell transplant

A stem cell transplant carries the risk of several complications. Some patients experience minimal problems, but others may develop complications that require treatment or hospitalisation.

The risk can depend on many factors, including your specific type of leukaemia, previously received 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 and initiate a stable production of the different blood cells. Your recovery is monitored by a progressive increase in the number of white blood cells and platelets in your blood.

Complications associated with allo-SCTs include:

Engraftment syndrome

Engraftment syndrome is thought to be an inflammatory condition at around the time your white blood cells are recovering after the transplant. It is characterised by the occurrence of a high non-infectious fever. The fever is usually associated with a rash, excess fluid in the lungs and diarrhoea.

Engraftment syndrome is a mild complication and, if properly diagnosed and treated, resolves within a few days.

Graft rejection

Graft rejection is the rejection of the donor cells by the recipient's immune system because the match between the donor and the recipient was not close enough.

There is usually an absence of the donor cells in the patient's bone marrow and the levels of all the patient's blood cells are very low.

Graft rejection is a major cause of graft failure.

Graft failure

This occurs when the

transplanted stem cells fail to start making new blood cells in the bone marrow. Primary graft failure is defined as no evidence of engraftment at 21-28 days after the transplant. Secondary graft failure is described as the loss of a previously functioning graft.

Graft failure is more common in patients who received HLA-mismatched grafts or who received reduced intensity/non-myeloablative conditioning.

Graft failure may be overcome by infusion of additional stem cells. The stem cells used for this second infusion may come from either the same donor or a different donor. Although uncommon, graft failure can be a major complication associated with a poor prognosis.

Your medical team will be monitoring your blood cell counts regularly. This means if you do start to show signs of graft failure you can get the best treatment straight away.

Graft-versus-host disease

Graft-versus-host disease following an SCT is when the T-cells from the donor recognise your own cells as foreign, and start an immunological attack against your healthy tissues.

This side effect is given special consideration in the next section (starting on page 28).

Cytomegalovirus (CMV)

CMV is a beta-herpes virus that infects the majority of people and does not cause any symptoms. After the infection, the virus remains latent ('sleeping') for life in the white blood cells in the blood and treatment is not required.

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.

Cataracts

This is a clouding of the lens of the eye, which causes vision loss. Cataracts may appear at five to six years after the transplant if you have received total body irradiation.

It is advisable that after a transplant you have annual eye tests. Cataracts are easily resolved with surgery.

Graft-versus-host disease

GVHD occurs when the T-cells from your donor attack your organs and tissues. When you first receive the cells from a donor, these cells do not recognise the HLA proteins on your own cells. They will consider your body as something foreign and will therefore react and attack your organs and tissues.

The greater the HLA mismatch between you and your donor, the greater the risk of developing GVHD. However, GVHD may occur even though you and your donor are fully compatible, since there are always minor differences in the HLA proteins between two individuals. The only exception to this is if donor and recipient are identical twins.

GVHD affects approximately 30–40% of recipients of allo-SCTs. 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 cyclosporine or a combination of the immunosuppressants mycophenolate mofetil and tacrolimus. After the transplant 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-cells from your donor's peripheral blood or bone marrow before the transplant. New therapeutic options for GVHD are constantly being developed, and your doctor can explain what the best option may be for you.

For most of the patients who go on to develop GVHD, corticosteroids remain the first-line treatment for both acute and chronic GVHD.

While developing GVHD may be a setback, it is important to remember that even though GVHD can impact on your quality of life, it does have some benefit. The same immune reaction that attacks your normal cells will also target and destroy any surviving cancer cells. Therefore, patients who develop GVHD have lower 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 some years later.

Acute GVHD

Acute GVHD mainly affects your skin, gastro-intestinal tract and liver. To confirm the diagnosis a tissue biopsy may be required. Depending on the number and severity of organs affected, GVHD is graded from one to four. Grade one represents a mild form of GVHD and may not require treatment and grade four represents the most severe form requiring treatment with corticosteroids and immunosuppressants.

Skin lesions

These lesions take the form of a rash resembling that of measles. It can affect your whole body and, exceptionally, it can turn into blisters and vesicles (small, fluid-filled sacs that can appear on your skin) similar to those of a burn.

Sickness and diarrhoea

These symptoms are a result of the involvement of your gastro-intestinal tract. You may be given anti-emetics to treat your sickness and painkillers if you have abdominal cramps. To avoid dehydration, you may be given intravenous fluids. If you can't eat and are losing weight you may be fed through a nasogastric tube, which is a tube running from the nose to the stomach.

Jaundice

This manifests itself as a yellowing of your eyes and skin due to 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 levels of red blood cells and platelets.

Chronic GVHD

Chronic GVHD occurs in 25–60% of recipients of allo-SCTs who are still alive six months after the transplant. Chronic GVHD normally occurs between three

Graft-versus-host disease (cont.)

and six months after the allo-SCT transplant, but its onset can occur as late as two years or more afterwards.

Chronic GVHD is a syndrome related to acute GVHD. It is more common in patients who have had acute GVHD; however, it does occur in 33% of patients who have not had the acute form. Chronic GVHD is more commonly seen in older patients and recipients of transplants using peripheral blood stem cells compared with bone marrow transplants.

Chronic GVHD has many symptoms similar to those of autoimmune disorders such as progressive systemic sclerosis, Sjögren's syndrome and primary biliary cirrhosis. Chronic GVHD might affect the skin, liver, eyes, mouth, lungs, gastrointestinal tract, neuromuscular system (your nerves and muscles) or genitourinary tract (your reproductive and urinary systems). The inflammatory symptoms are similar to those with acute GVHD, but, as the condition becomes chronic, tissue fibrosis and greater organ involvement develops.

The most common symptoms of chronic GVHD include:

Skin lesions

One of the earliest signs of GVHD is a rash on the palms of the hands or the soles of the feet. It is often dry and itchy and may spread to the rest of the body. As with acute GVHD, it can turn into blisters and your skin can appear similar to a burn in severe cases. With chronic GVHD, scleroderma, characterised by a hardening of your skin, can develop.

Abdominal swelling and jaundice due to liver injury

Abdominal swelling, jaundice and abnormal liver function test results will indicate that the liver is scarred and has been damaged.

Dry eye syndrome

This consists of dry mouth and/or a gritty sensation in your eyes. These symptoms 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 when swallowing and weight loss

You might find it uncomfortable to swallow or experience pain 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 burning or bleeding on passing water is an indication that your genitourinary system is affected.

Other symptoms

Other less common symptoms which do not respond well to treatment and can become chronic problems are:

- Fasciitis: inflammation of the connective tissue around the muscles, blood vessels and nerves
- Bronchiolitis obliterans syndrome: obstruction of small airways in the lungs due to inflammation
- Oral ulcers which do not respond to topical therapies

If you develop chronic GVHD you may be given long-term immunosuppressants.

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?

You will 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. Additional 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 an allo-SCT, you are effectively receiving a new immune system that will develop from the transplanted stem cells. For the transplanted T-cells to become effective in defending your organism, they need a period during which they can increase in numbers and learn to recognise foreign agents.

For this reason, you must be revaccinated. You will start your vaccinations approximately 6 to 12 months after your transplant. In patients with active GVHD, who are receiving corticosteroid treatment or immunosuppressants, vaccinations may be delayed until their body can develop the antibodies to the vaccines.

Compulsory vaccines are those for pneumococcus, hepatitis A and B, haemophilus influenzae, diphtheria, tetanus, pertussis, polio (inactivated), measles, rubella and mumps.

Also, once discharged, you may need to return to hospital for the treatment of some complications.

The more frequent causes for rehospitalisation are insufficient fluid intake, infections and GVHD. Hospital readmissions in the first three to six months after the transplant 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

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 a while (relapse).

Graft rejection or failure 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 your transplant, and are less common after five years. You will have regular checks to ensure 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-cells to try and enhance the anti-leukaemia effect.

Some patients may not be able to have further treatment because of the high risk, whereas 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

Acute lymphoblastic leukaemia (ALL)

A leukaemia in which the lymphocyte cells start multiplying uncontrollably in the bone marrow resulting in high numbers of abnormal, immature lymphocytes called blasts. Lymphocytes are a type of white blood cell involved in the immune response.

Acute myeloid leukaemia (AML)

A rapid and aggressive cancer of the myeloid cells in the bone marrow.

Allogeneic stem cell transplant (allo-SCT)

A transplant of stem cells from a matching donor.

Anaemia

A condition where the number of red blood cells are reduced. Red blood cells contain haemoglobin and transport oxygen to the body's cells. Anaemia may be due to a lack of iron, leukaemia, or sickle cell disease.

Antibiotic

A drug that inhibits the growth of, or destroys, bacteria.

Antibody

The large Y-shaped protein produced by B-cell lymphocytes in response to a specific antigen, such as a bacteria, virus, or a foreign substance in the blood.

Antigen

A toxin or other foreign substance which induces an immune response in the body, especially the production of antibodies.

Autoimmune disease

A disorder where healthy cells are destroyed by the body's own immune system.

Autologous stem cell transplant (auto-SCT)

A transplant of stem cells derived from the same individual.

Bone marrow biopsy

A bone marrow biopsy involves the collection of a sample of bone marrow from the hip bone, generally under local anaesthesia. A bone marrow surgical instrument with a cylindrical blade, called trephine, is used to remove a 1 or 2 cm core of bone marrow in one piece.

Chemotherapy

Drugs that work in different ways to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.

Chronic lymphocytic leukaemia (CLL)

A leukaemia in which the B-lymphocyte cells in the bone marrow start multiplying uncontrollably leading to large numbers of abnormal, immature cells called 'blasts', which prevent the bone marrow from producing enough healthy blood cells of all types.

Chronic myeloid leukaemia (CML)

A leukaemia in which the myeloid cells start multiplying in the bone marrow leading to large numbers of abnormal, immature myeloid cells called 'blasts', which prevent the bone marrow from producing enough healthy blood cells of all types.

Conditioning regimen

The use of a chemotherapy regimen or total body irradiation to eliminate cancer cells and prevent the immune system rejecting the new stem cells prior to an allogeneic stem cell transplant.

Engraftment

The process by which stem cells from a donor physically attach to your bone marrow. They then multiply and make new blood cells.

Granulocyte-colony stimulating factor (GCSF)

A growth factor required to stimulate the growth of blood stem cells.

Haematopoiesis

The process by which blood cells are formed.

Hepatitis

Inflammation of the liver which may be a result of damage or a viral infection.

Human immunodeficiency virus (HIV)

A virus which attacks the cells in the immune system and weakens the body's ability to fight everyday infections and diseases.

Immunosuppressants

Drugs that reduce or suppress the strength of the immune system.

Immunotherapy

Treatment that uses the body's own immune system to fight the cancer.

Irradiation

Irradiation is the process by which an object is exposed to radiation.

Glossary (cont.)

Jaundice

A yellow tinge in the skin and white of the eyes which is caused by a build-up of bilirubin, a waste material, in the blood normally excreted in the bile and urine. An inflamed liver or obstructed bile duct can lead to jaundice.

Mucositis

The painful inflammation and ulceration of the mucous membranes lining the digestive tract.

Palliative care

Also known as supportive care, this is a type of care that focusses on improving the quality of life for a patient with a life threatening illness and their loved ones.

Plasma cell

A type of white blood cell that produces antibodies and is derived from a B-cell lymphocyte. It is an ovoid (egg-shaped) cell with an off-centre nucleus.

Platelets

Small blood cells that help the body form clots to stop bleeding.

Radiation

The release of energy in the form of particles or waves.

Radiation treatment

Cancer treatment that uses high doses of irradiation to kill cancer cells and shrink tumours.

Red blood cells

Small blood cells that contain haemoglobin and carry oxygen and other substances to all tissues of the body.

Relapse condition (e.g. leukaemia)

Relapse occurs when a patient initially responds to treatment, but after six months or more, the response stops. This is also sometimes called a recurrence.

Stem cell

The most basic cell in the body that has the ability to develop into any of the body's specialised cell types, from muscle cells to brain cells.

Targeted therapy

Drugs that specifically interrupt leukaemia/cancer cells from growing in the body. These drugs do not simultaneously harm healthy cells the way conventional chemotherapy drugs do.

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
support@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

support@leukaemiacare.org.uk

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

Leukaemia Care is registered as a charity in England and Wales (no.1183890) and Scotland (no. SC049802).
Company number: 11911752 (England and Wales).
Registered office address: One Birch Court, Blackpole East, Worcester, WR3 8SG

Leukaemia Care
YOUR Blood Cancer Charity