



Transplants in Lymphoma

OVERVIEW

A type of treatment that some people can receive for their lymphoma is a Stem cell or Bone Marrow transplant. Stem cell transplants are sometimes used to treat lymphoma patients who are in remission or who have a relapse during or after treatment. Stem cell transplants allow doctors to use higher doses of chemotherapy to kill the lymphoma than what would normally be tolerated. Radiation is sometimes given as well. This treatment can kill the cancer cells but also destroys the bone marrow, which prevents new blood cells from being formed. A stem cell is an immature cell in the bone marrow that can develop into mature blood cells. These cells maintain a person's blood cells, replacing older or damaged cells with newer ones. The stem cells can be a person's own stem cells (an autologous stem cell transplant) or they can be from a donor (an allogeneic stem cell transplant). If given donor stem cells, these can also form a new immune system that can recognise and fight the lymphoma.

WHEN A TRANSPLANT IS INDICATED

Stem cell transplants are used in different situations but mainly when the:

- Lymphoma has relapsed (come back) after treatment and responded to further (known as salvage) therapy
- Lymphoma is refractory (doesn't respond) to initial treatment but responded to salvage therapy
- As part of your first treatment if you have achieved remission but the doctors think the lymphoma is likely to relapse

Because high-dose chemotherapy and stem cell transplantation may place great strain on a person's body, they are not options for everyone. Additionally, a long hospital stay is often involved. In deciding if transplantation is a good option, doctors will consider many factors, including the person's health status, age, medical history, stage of the lymphoma, and response to previous therapy. The latter is very important as transplants don't work (and hence are not done) in patients with progressive lymphoma resistant to chemotherapy.

SOURCES OF STEM CELL FOR TRANSPLANTATION

The transplanted stem cells come from two main sources:

Autologous: stem cells are collected from the blood of the patient using a procedure called apheresis.

Allogeneic (from a donor):

1. **Peripheral blood:** Currently, stem cells collected from blood are most commonly used in stem cell transplantations. A procedure called apheresis is used to collect stem cells from the blood.
2. **Bone Marrow** is the wet, spongy tissue inside bones where blood cells are generated. Bone marrow stem cells can be collected under anaesthesia from the pelvis or hip bone. This procedure is now rarely used in transplants.
3. **Umbilical Cord Blood:** After the birth of a newborn, some of the baby's blood is left behind in the placenta and umbilical cord. This is known as cord blood. This blood can be collected and frozen until needed for later use in a stem cell transplant. Stem cell transplantations with umbilical cord blood are not as common as those from other sources.

TYPES OF TRANSPLANTS

Often the terms Bone Marrow Transplant and a Stem Cell Transplant are used interchangeably so what is the difference? The difference between the two depends on where the stem cells are taken from. In bone marrow transplants, the stem cells are taken directly from the bone marrow. In stem cell transplants, the stem cells are taken from the circulating blood. Stem cell transplants are also known as peripheral blood stem cell transplants (PBSCs). PBSCs are now more commonly performed than bone marrow transplants, as the procedure is easier to do and the body is able to regenerate new stem cells faster. Bone marrow transplants are very rare, and are only used in certain circumstances. There are 2 main types of stem cell transplants (SCTs) based on the source of the stem cells:

Autologous Stem Cell Transplantation uses a person's own stem cells. The stem cells are collected after a cycle of treatment

of high dose chemotherapy, and often people have 2 cycles of treatment before the stem cells are collected. A procedure called apheresis is used to collect stem cells from the blood. Then the stem cells are frozen, stored and given back after high-dose treatment (transplant).

Allogeneic Stem Cell Transplantation uses stem cells from a donor (someone else) such as a close relative (brother or sister, known as a matched related donor (MRD)) or a matched unrelated donor (MUD) from one of the many donor registries around the world. Rarely a transplant can be performed from an umbilical cord donor (see above). These transplants may work in two ways: the effect of the high dose chemotherapy (as in an autograft) PLUS the potential for a graft vs lymphoma effect in which the new immune system of the donor may recognise any remaining lymphoma cells as being different, and attack and eradicate them. This is called a graft vs lymphoma effect. It is important to note that this effect does not always occur (ie. the lymphoma cells may be resistant to attack by the donor cells) and it may be associated with graft versus host disease in which the donor's immune system attacks normal parts of the body such as skin, liver, lungs and the gut.

Allogeneic stem cell transplants are not commonly performed in patients with lymphomas. They are sometimes utilised in patients who have relapsed after an autologous stem cell transplant and are most often used in patients who have indolent lymphomas.

THE TRANSPLANTATION PROCESS

There are four major steps that are involved in a transplant:

1. **Collection of Stem Cells:** Harvesting is the procedure by which the stem cells are obtained in preparation for the transplant. The person is connected to an apheresis machine and the blood is removed and returned via a central line. In a PBSCT, stem cells are taken from the bloodstream, a far easier and more commonly used procedure. This requires the use of injections (filgrastim or G-CSF) to push (or mobilise) the stem cells from the bone marrow into the peripheral blood. The stem cells are separated from other components of the blood in a process called apheresis, with the rest of the blood being returned to the patient. The less common approach is a bone marrow harvest, this is where the stem cells are withdrawn from the bone marrow under general anaesthesia by inserting a needle into a bone in the pelvic region, called the iliac crest. This bone marrow is then filtered and stored until the day of the transplant.
2. **Processing/preserving the stem cells or bone marrow:** Stem cells or bone marrow harvested from the patient

(autologous transplant) are generally preserved and stored in a freezer until ready for use. Stem cells from a donor (allogeneic transplant) are usually collected immediately before use or stem cells from a donor may be collected and frozen until they are ready to be used.

3. **Admission to hospital for Transplant:** High-dose chemotherapy, with or without radiation therapy, is then administered. The intent is to destroy any residual lymphoma cells, but this is at the expense of destroying the healthy cells in the marrow. Depending on which transplant you have, admission into hospital can be from three to six weeks.
4. **Reinfusing stem cells:** After the intensive chemotherapy has finished, the stem cells are reinfused into the patient. These stem cells slowly begin to produce new, healthy blood cells. Eventually, they will produce enough healthy cells to repopulate the whole bone marrow, replenishing all blood and immune cells. In allogeneic stem cell transplants as these donated cells take hold (or engraft) in the recipient (patient), they begin to function as part of the immune system and may attack the lymphoma cells. This is termed graft-versus-tumour effect. In some cases, following allogeneic transplant, the donor cells also attack the patient's healthy cells. This is called graft-versus-host disease (GVHD).

After having the cells infused, the process where the immune system begins to produce new healthy cells can take weeks. During this process patients need to stay in hospital which can be from three to six weeks. The patient is kept in a protected environment to minimize infection. Risk of developing a severe, potentially life-threatening infection is highest two to three days following transplant until the stem cells have been able to repopulate the immune system, usually in about two to four weeks. This is faster with an autologous transplant than an allogeneic transplant.

During the first month following transplant, the transplanted cells will start to grow and produce healthy blood stem cells that appear in the blood. This process is referred to as engraftment. Frequent blood tests may be done to monitor this process. Complete recovery of immune function may take up to several months for autologous transplant recipients and one to two years for patients receiving allogeneic transplants. It is very important for patients to take precautions to avoid infections, including washing hands diligently, avoiding crowds, cooking all food, avoiding fresh flowers, gardening, swimming, and not sleeping with pets.

SIDE EFFECTS OF TRANSPLANTATION

After high-dose chemotherapy treatment, blood cell counts

FACT SHEET

are low. This increases a patient's risk of infection and reduces the ability of the blood to clot, potentially increasing the risk of bleeding. Also, because chemotherapy doses are higher, side effects from the chemotherapy such as nausea, vomiting, fatigue, mouth sores, and loss of appetite may be more intense, especially immediately following transplantation and for a couple of weeks thereafter.

Patients receiving a stem cell transplant may also experience long term side effects, including potential infertility, early menopause, damage to the thyroid gland, cataracts, or damage to the lungs or bone.

With allogeneic stem cell transplantation, there is a risk of GVHD, GVHD is a common side effect, and while it is often mild, it may cause very serious complications.

FOLLOW UP

Once the stem cell transplant is completed, people with lymphoma need to be followed up closely by their specialist with regular appointments to monitor:

- Evaluate the effectiveness of the transplant
- Ongoing transplant side effects
- Recovery from transplant
- Signs of lymphoma relapsing
- Potential late effects caused by the transplant that can occur months or years later, that can be based on the duration and frequency of transplant and prior treatments, age, gender and overall health of each person

RESOURCES AND SUPPORT

Organisation	How can they help?
Lymphoma Australia	<ul style="list-style-type: none"> • Lymphoma Australia offers a wide variety of resources and support for people with lymphoma or CLL and their carergivers. Please visit lymphoma.org.au for further information: • Lymphoma Australia Fact sheets & booklets including: <ul style="list-style-type: none"> • Lymphoma: what you need to know • Autologous stem cell transplants • Allogeneic stem cell transplants • Lymphoma subtypes • Emotional impact of a lymphoma diagnosis & treatment

Organisation	How can they help?
	<ul style="list-style-type: none"> • Lymphoma Australia YouTube Channel: Presentations and interviews on a variety of topics about lymphoma subtypes, management and supportive care. Including: Transplants in lymphoma, presented by Dr Nada Hamad, St Vincent's Hospital, Sydney youtube.com/user/LymphomaAustralia • Lymphoma Nurse Support Line: 1800 953 081 or email: nurse@lymphoma.org.au • Online private Facebook group: Lymphoma Down Under

SOME QUESTIONS TO ASK YOUR DOCTOR

- Am I able to be considered for a stem cell transplant?
- What type of transplant would be appropriate for me?
- What type of side effects should I expect?
- How long will I be in hospital for if I have a transplant?
- Can I get my family tested to see if they are a match?