LYMPHOMA
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Getting the Facts

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Transplant in Lymphoma

Stem Cell Transplantation as a Treatment for Lymphoma

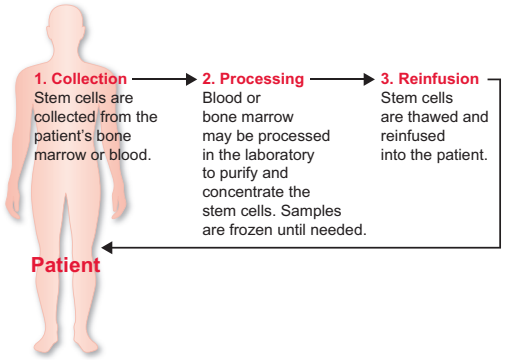
A stem cell is an immature cell in the bone marrow that can develop into mature blood cells. These cells maintain a person's blood cells, replacing older or damaged cells with newer ones. High-dose chemotherapy treatment can cause significant damage to stem cells in the bone marrow, compromising a person's ability to renew their blood cells. The ability to transplant stem cells allows physicians to use higher doses of chemotherapy to treat the cancer than the body would normally tolerate, increasing the probability of killing cancer cells. If the chemotherapy is followed by an infusion of stem cells, these new stem cells can replace the cells in the bone marrow that were destroyed during the chemotherapy treatment.

Because high-dose chemotherapy and stem cell transplantation may place great strain on a patient's body, they are not options for everyone. This procedure is typically used for patients with relapsed (disease returns after treatment), aggressive lymphoma that is still sensitive to the effects of chemotherapy. The procedure does not work for patients with tumors that are unresponsive to drugs. Additionally, a long hospital stay is often involved. In deciding if transplantation is a good option, doctors will consider many factors, including the patient's health status, age, medical history, cancer stage, and response to previous therapy.

Types of Stem Cell Transplantations

Autologous Stem Cell Transplantation

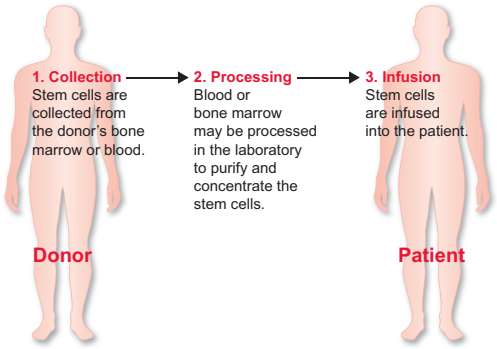
In *autologous stem cell transplantation*, stem cells are donated by the patient and collected and frozen before the patient undergoes cancer treatment. After cancer treatment is given and the cancer cells are believed to be gone, the collected stem cells are reinfused back into the patient.



Because a patient is receiving their own stem cells, an autologous stem cell transplant ensures a perfect match between the patient and the transplanted cells, which improves outcomes. Additionally, this procedure has a lower risk of transmitting blood-borne infectious diseases.

Allogeneic Stem Cell Transplantation

In *allogeneic stem cell transplantation*, the stem cell donor is not the patient, but is another person who is genetically similar—often a brother or sister. However, it is possible for the donor to be a person unrelated to the patient. After the patient has undergone chemotherapy and/or radiation therapy, the donor's stem cells are infused into the patient. 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 cancer cells. This is termed graft-versus-tumor effect, which only occurs in allogeneic stem cell transplants. In some cases following allogeneic transplant, the donor cells also attack the patient's healthy cells. This is called graft-versus-host disease (GVHD). The more closely related the donor's cells are to the patient's, the less likely this is to occur.



Reduced-intensity transplantation (also called non-myeloablative or mini-allogeneic transplantation) is a type of allogeneic transplantation. Compared with a standard allogeneic transplant, a reduced-intensity transplant uses lower doses of chemotherapy and/or radiation to prepare the patient for the transplant. These types of transplants are used in patients with adverse health conditions or those with more advanced age, which are factors that put them at higher risk when their bone marrow is destroyed during standard high-dose chemotherapy (with or without radiation). The reduced-intensity treatment kills some of the cancer cells and some of the

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bone marrow, and it suppresses the patient's immune system just enough to allow the donor's stem cells to settle in the bone marrow. The patient's own stem cells are not all killed, and their blood cell counts do not fall as low as they do with high-dose chemotherapy. The cells from both the donor and the patient exist together in the patient's body for some time, but the donor's cells eventually take over the bone marrow and replace the patient's own bone marrow cells over the course of months. The new cells from the donor can then develop an immune response to the cancer and help kill the remaining cancer cells.

Sources of Stem Cells for Transplantation

Identifying a Donor

If donor stem cells are used for allogeneic transplantation, it is important to ensure that the donor's blood cells are as similar to the patient's as possible. If the stem cells are too different, the new immune cells from the transplantation will try to destroy cells in the patient's body, leading to GVHD—a serious condition. Before a transplant, HLA typing (also called tissue typing) is performed with blood tests to check the surface of the blood cells for proteins called HLA markers or histocompatibility antigens. The proteins on the outside of the cells are compared. Close family members are more likely to have similar patterns of proteins. A mismatched transplant is more likely to cause GVHD after the transplant.

Stem cells for transplantation can be obtained from three sources: bone marrow, peripheral blood, and umbilical cord blood.

Bone Marrow

Bone marrow is a wet, spongy tissue inside bones where blood cells are generated. Bone in the pelvis, or hip bone, is a good source of stem cells, and cells from this bone are most often used for a bone marrow transplant. Bone marrow stem cells can be used for both autologous and allogeneic stem cell transplantations.

To remove the stem cells, the person whose stem cells are being collected (the donor) is given general anesthesia. A large needle is then inserted into the back of the hip bone and some of the bone marrow is removed and frozen. The marrow that is removed (harvested) is passed through a series of filters to remove bone or tissue fragments and then placed in a plastic bag from which it can be infused into the recipient's vein, usually within a few hours. Alternately, the marrow can be frozen and stored for years.

When it is time for the patient to receive the stem cells, the marrow is given through a vein, just like a blood transfusion. A hospital stay of about six to eight hours after the procedure can be expected in order to recover from the anesthesia and the pain at the needle insertion sites. Lower back soreness may be experienced for a few days following the procedure. The donor's bone marrow is regenerated soon after the procedure. The loss of red blood cells may result in temporary anemia, which can be managed with iron supplements.

Peripheral Blood

Currently, stem cells collected from blood are most commonly used in stem cell transplantations. Normally, only a few stem cells are found in the blood. A drug called granulocyte colony-stimulating factor, or G-CSF (filgrastim, lenograstim, and pegfilgrastim), is given to stimulate stem cell growth and improve the ability to collect an appropriate number of stem cells.

To collect the stem cells, the blood is removed through a catheter, the stem cells are collected, and the rest of the blood is returned to the donor. This process is called apheresis. The entire procedure takes three to four hours but needs to be repeated several times. The stem cells are treated to remove contaminants and are then frozen to keep them alive until the patient is ready to receive them.

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. This is because there are a smaller number of stem cells present and cord blood transplants can take longer to engraft (enter the marrow to replace the damaged stem cells) and start working. Umbilical cord blood stem cell transplants can be considered for children or small-sized adults and in situations where a well-matched donor could not be found among family members or people who have signed up to donate.

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The Transplantation Process

Once donor stem cells have been obtained, patients undergoing stem cell transplant will experience a similar procedure whether they are undergoing an autologous transplant or an allogeneic transplant.

Transplants are preceded by chemotherapy treatment to inactivate the immune system and reduce the tumor burden, killing malignant cells. This process is called preparatory therapy and may include conditioning treatment that destroys the patient's stem cells. These preparative treatments are extremely toxic and may contain radiation. Total body irradiation with etoposide and/or cyclophosphamide chemotherapy may be used. The total body irradiation may be "fractionated," meaning that the radiation dose is given over several days. This approach decreases the toxicity. In patients unable to undergo total body irradiation, BEAM (carmustine, etoposide, cytarabine, and melphalan) and CBV (cyclophosphamide, carmustine, and etoposide) are two commonly used regimens. Monoclonal antibodies, such as rituximab, may also be used.

Additionally, a surgeon or radiologist may implant a long, thin tube (intravenous catheter) in the chest near the neck. The catheter is normally surgically placed after giving local anesthesia to numb the insertion area. The catheter, often called a central line, usually remains in place for the duration of treatment. This central line is used to infuse the transplanted stem cells and other medications and blood products into the body.

A few days after treatment, the patient is given the stored stem cells. Donor stem cells are delivered through the catheter. Infusing the stem cells usually takes several hours. Patients may experience a fever, chills, hives, shortness of breath, or a drop in blood pressure during the procedure. To stimulate the growth of infection-fighting white blood cells, G-CSF may be given. Additionally, blood cell replacement, nutritional support, and drugs to treat GVHD may be used. Hospital stays can be three to five 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 a blood transplant than a bone marrow transplant.

It is very important for patients to take precautions to avoid infections, including ensuring vaccinations are up to date prior to transplant, washing hands diligently, avoiding crowds, cooking all food, avoiding fresh flowers, gardening, and swimming, and not sleeping with pets.

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.

Side Effects

After high-dose chemotherapy treatment with or without radiation, blood cell counts are low, which 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. There is also a risk of developing leukemia. With allogeneic stem cell transplantation, there is a risk of GVHD, which is common and can either be a minor problem or a very serious one. It is usually controlled with drugs that suppress the immune cells to keep them from attacking the patient's cells.

Patients receiving reduced-intensity transplantation may avoid some of the side effects associated with high-dose chemotherapy, although there is still an increased risk of serious side effects, compared with autologous stem cell transplantation, due to the potential for GVHD.

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Follow-up

Patients in remission should have regular visits with a physician who is familiar with their medical history and the treatments they have received. Medical tests (such as blood tests and computed axial tomography [CAT] scans) may be required at various times during remission to evaluate the need for additional treatment. Some treatments can cause long-term effects or late effects, which can vary based on duration and frequency of treatments, age, gender, and the overall health of each patient at the time of treatment. A physician will check for these effects during follow-up care.

Patients and their caregivers are encouraged to keep copies of all medical records and test results as well as information on the types, amounts, and duration of all treatments received. This documentation will be important for keeping track of any effects resulting from treatment or potential disease recurrences.

Support

A lymphoma diagnosis often triggers a range of feelings and raises concerns. In addition, cancer treatment can cause physical discomfort. Support groups and online message boards can help patients connect with other people who have lymphoma. One-to-one peer support programs, such as the Lymphoma Research Foundation's (LRF) Lymphoma Support Network, match lymphoma patients (or caregivers) with volunteers who have gone through similar experiences.

Resources

LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma. LRF also provides many educational activities, from in-person meetings to teleconferences and webcasts, as well as E-Updates that provide the latest disease-specific news and treatment options. For more information about any of these resources, visit our website at www.lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.