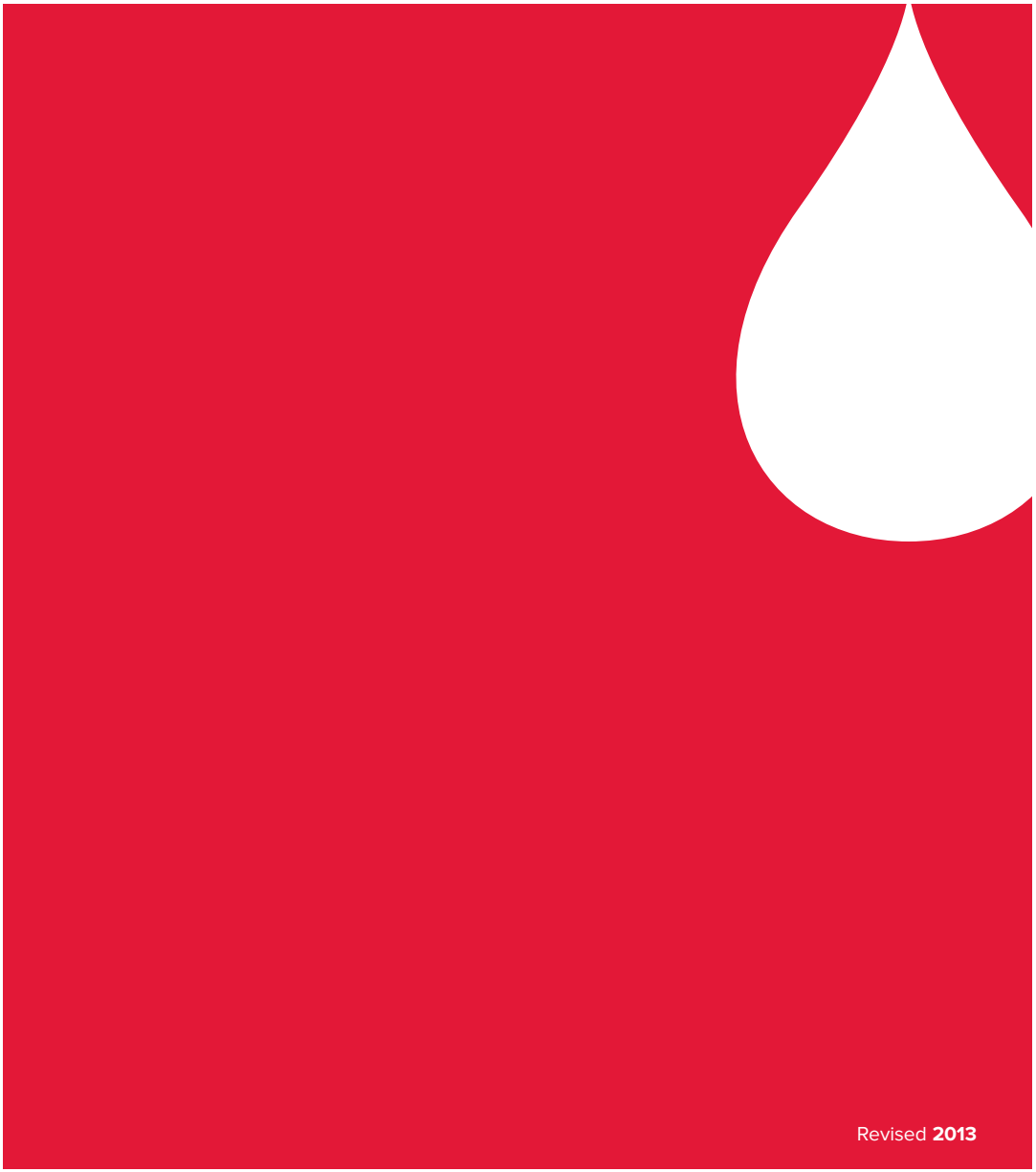
LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

someday is today®

Blood and Marrow Stem Cell Transplantation



Revised **2013**

LEUKEMIA & LYMPHOMA SOCIETY®

Booklet Updates

The Leukemia & Lymphoma Society wants you to have the most up-to-date information about blood cancer treatment. To read about new treatments that have been FDA approved since this booklet was printed, visit www.LLS.org/bookletupdates.

If you do not have access to the internet, or for more information, contact an Information Specialist at (800) 955-4572 or infocenter@lls.org.

A Message from Louis J. DeGennaro, PhD

President and CEO of The Leukemia & Lymphoma Society

The Leukemia & Lymphoma Society (LLS) is the world's largest voluntary health organization dedicated to finding cures for blood cancer patients. Our research grants have funded many of today's most promising advances; we are the leading source of free blood cancer information, education and support; and we advocate for blood cancer patients and their families, helping to ensure they have access to quality, affordable and coordinated care.

Since 1954, we have been a driving force behind nearly every treatment breakthrough for blood cancer patients. We have invested more than $1 billion in research to advance therapies and save lives. Thanks to research and access to better treatments, survival rates for many blood cancer patients have doubled, tripled and even quadrupled.

Yet we are far from done.

Until there is a cure for cancer, we will continue to work hard—to fund new research, to create new patient programs and services, and to share information and resources about blood cancer.

This booklet has information that can help you understand your finances, prepare questions, find answers and resources, and communicate better with members of your healthcare team.

Our vision is that, one day, all people with blood cancers will either be cured or will be able to manage their disease so that they can experience a better quality of life. Today, we hope our expertise, knowledge and resources will make a difference in your journey.

Louis J. DeGennaro, PhD
President and Chief Executive Office
The Leukemia & Lymphoma Society

(Letter updated March 2015)

Table of Contents

Acknowledgements

For her critical review of *Blood and Marrow Stem Cell Transplantation* and important contributions to the material presented in this publication, LLS gratefully acknowledges

Jane Liesveld, MD
Professor, Department of Medicine, Hematology/Oncology
Clinical Director, Blood and Marrow Transplant Program
University of Rochester Medical Center
Rochester, NY

LLS also gratefully acknowledges members of the staff of the Center for International Bone Marrow Transplant Research, members of the staff of the National Bone Marrow Transplant Link (nbmtLINK) and members of the staff of Be The Match®, operated by the National Marrow Donor Program® for their important contributions to the material presented in this publication.

Introduction

A stem cell transplant is a procedure that replaces unhealthy blood-forming cells with healthy ones. This booklet provides information about blood and marrow stem cell transplantation for the treatment of blood cancers (leukemia, lymphoma, myeloma, myelodysplastic syndromes and myeloproliferative neoplasms). Stem cell transplantation procedures continue to be improved, making transplantation a treatment option for more patients. Certain other marrow disorders are also treated with transplantation, and many of the principles are the same as those described in this booklet. For some patients, this complex procedure offers a curative treatment option.

Blood and Marrow Stem Cell Transplantation includes definitions of medical terms. Some of the terms used in this booklet are synonyms for other terms used by healthcare professionals. Check with your doctor if you have questions about how the terms used in this booklet apply to you.

Here to Help

This booklet will give you suggestions to help you take care of yourself and help you talk to your doctor. We encourage you to take the lead in asking questions and discussing your fears and concerns. These actions will give members of your healthcare team the opportunity to answer your questions, extend emotional support and provide any needed referrals.

A blood cancer diagnosis is often a shock to the patient, family members and friends. Denial, depression, hopelessness and fear are some of the reactions people may have. Keep in mind that

- Many people are better able to cope once they begin treatment and can look forward to recovery
- The outlook for people with blood cancers is continuing to improve. New approaches to therapy are being studied in clinical trials for patients of all ages and at every stage of treatment.

LLS Has Ways to Help. Your treatment may affect your daily life, at least for a time. You may have questions about your treatment and want to have friends, family members or caregivers help you get information.

Making treatment choices, paying for medical care, communicating with healthcare providers, family members and friends—these are some of the stresses that go along with a cancer diagnosis. LLS offers free information and patient services for individuals and families touched by blood cancers.

Speak to an Information Specialist. Information Specialists are master's level oncology professionals. They provide accurate, up-to-date disease and treatment information and are available to speak with callers Monday through Friday, from 9 a.m. to 6 p.m. ET at (800) 955-4572. You can email infocenter@LLS.org or chat live with a Specialist at www.LLS.org.

Clinical Trials. Our Information Specialists help patients work with their doctors to find out about specific clinical trials. Information Specialists conduct clinical-trial searches for patients, family members and healthcare professionals. You can also use an online clinical-trial search service supported by LLS that offers patients and caregivers immediate access to listings of blood cancer clinical trials. Please see www.LLS.org/clinicaltrials.

Advocacy and Public Policy. The LLS Office of Public Policy (OPP) enlists volunteers to help advocate for policies and laws to speed the development of new treatments and improve access to quality medical care. Visit www.LLS.org/advocacy to find out more or get involved.

Language Services. Free language services are available when you speak with an Information Specialist. Let your doctor know if you want a professional healthcare interpreter who speaks your native language or uses sign language to be present during your visit. Many times, this is a free service.

Información en Español. LLS has a number of resources available in Spanish for patients, caregivers and healthcare professionals. You can read and download these resources online at www.LLS.org/espanol or order printed copies by mail or by phone.

Co-Pay Assistance Program. This program offers assistance for financially eligible patients with certain blood cancer diagnoses to help pay for private or public health insurance premiums and/or co-pay costs for prescription medications. Check www.LLS.org/copay or call (877) 557-2672 to speak to a *Co-Pay Assistance Program* specialist for more eligibility information.

Free Materials. LLS publishes many free education and support materials for patients and healthcare professionals. PDF files can be either read online or downloaded. Free print versions can be ordered. Visit www.LLS.org/resourcecenter.

Chapter Programs and Services. LLS chapter offices around the United States and Canada offer support and education. Your chapter can arrange for peer-to-peer support through the *Patti Robinson Kaufmann First Connection Program*. The *Patient Financial Aid* program offers a limited amount of financial aid for qualified patients. Find your chapter by calling (800) 955-4572 or by visiting www.LLS.org/chapterfind.

Other Helpful Organizations. Our website, www.LLS.org/resourcedirectory, offers an extensive list of resources for patients and families about financial assistance, counseling, transportation, summer camps and other needs.

Telephone/Web Education Programs. LLS provides a number of free, live telephone and web education programs presented by experts for patients, caregivers and healthcare professionals. For more information, visit www.LLS.org/programs.

School Reentry. The *Trish Greene Back to School Program for Children With Cancer* is a program designed to increase communication among healthcare professionals, school personnel, parents and patients to assure children with cancer a smooth transition back to school. For more information, visit www.LLS.org/backtoschool.

Suggestions From Other People Living With Cancer

- Get information about choosing a cancer specialist or treatment center.
- Find out about financial matters: What does your insurance cover? What financial assistance is available to you?
- Learn about the most current tests and treatments for your type of blood cancer.
- Keep all appointments with the doctor and talk openly about your fears, concerns and/or any side effects that you experience.
- Talk with family and friends about how you feel and how they can help.
- Contact your doctor if you have fatigue, fever, pain or sleep problems so that any issues can be addressed early on.
- Get medical advice if you have experienced changes in mood, feelings of sadness or depression.

Reach Out. You and your loved ones can reach out for support in several ways.

- LLS offers online blood cancer discussion boards as well as online chats at www.LLS.org/getinfo.
- Local or Internet support groups and blogs can provide forums for support.
- Patients with cancer often become acquainted with one another, and these friendships provide support.

Information for Veterans. Veterans with certain blood cancer diagnoses who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs. For more information call the Department of Veterans Affairs at (800) 749-8387 or visit www.publichealth.va.gov/exposures/agentorange.

Information for World Trade Center Responders and Survivors. Responders, workers, and volunteers who helped with rescue, recovery, and cleanup at the World Trade Center and related sites in New York City; survivors who were in the New York City disaster area, lived, worked, or were in school in the area; and responders to the Pentagon and the Shanksville, PA crash who have been diagnosed with a blood cancer may be eligible for help from the World Trade Center Health Program. For more information, call the World Trade Center Health Program at (888) 982-4748 or visit www.cdc.gov/wtc.

Depression. Treatment for depression has proven benefits for people living with cancer. Depression is an illness that should be treated even when a person is undergoing cancer treatment. Seek medical advice if your mood does not improve over time—for example, if you feel depressed every day for a two-week period. Contact LLS or ask your healthcare team for guidance and referrals to other sources of help, such as counseling services or community programs. For more information you can contact the National Institute of Mental Health (NIMH) at www.nimh.nih.gov and enter "depression" in the search box at the top of the web page, or call the NIMH toll-free at (866) 615-6464.

We'd Like to Hear From You. We hope this booklet helps you. Please tell us what you think at www.LLS.org/publicationfeedback. Click on "LLS Disease & Treatment Publications—Survey for Patients, Family and Friends."

Overview and Types of Stem Cell Transplantation

Stem cell transplantation is a procedure that can restore marrow function for patients who have had severe marrow injury or abnormalities of the immune system. Marrow injury can occur because of primary marrow failure, destruction or replacement of marrow by disease, or intensive chemical or radiation exposure.

Fast Facts About Stem Cell Transplantation

- Since blood and marrow are both good sources of stem cells for transplantation, the term "stem cell transplantation" has replaced "bone marrow transplantation" as the general term for this procedure. The abbreviation "BMT" is now used to represent blood and marrow transplantation. There are many terms for transplantation, including bone marrow transplantation (BMT), marrow or cord blood transplantation or hematopoietic cell transplantation (HCT). These are all different names for the same procedure.
- Today, the stem cells used for transplantation can come from marrow, peripheral blood or umbilical cord blood. Peripheral blood is now the most common source of stem cells for transplantation.
- The use of cord blood stem cells for transplantation is about two decades old. Compared to peripheral blood or marrow, cord blood is a relatively new source of cells, especially for adults.
- "Reduced-intensity" allogeneic stem cell transplantation is an option for certain patients who have a stem cell donor. Compared to a fully myeloablative allogeneic transplant (referred to as a "standard" allogeneic transplant throughout this booklet; see page 24), a reduced-intensity transplant delivers lower doses of chemotherapy drugs and/or radiation to the patient in preparation for the transplant. The success of reduced-intensity transplantation depends upon the graft-versus-tumor (GVT) effect of the donor stem cells, rather than on high doses of chemotherapy. This approach may benefit older and sicker patients and other selected patients.
- The donor cells are called the "graft." When the donor cells attack the diseased cells, it is called the "graft-versus-disease (GVD) effect."
- Attempts to use the marrow cells of a healthy individual to restore the lost marrow function of another person began about 65 years ago.
- The basis for stem cell transplantation is that all blood cells and immune cells arise from stem cells in marrow. At the turn of the 20th century, scientists began to formulate the idea that a small number of cells in the marrow might be responsible for the development of all blood cells. They began to refer to them as "stem cells." The scientific exploration of marrow transplantation as a form of treatment began at the end of World War II.

- The source for the earliest transplants was the marrow of a healthy donor who had the same tissue (human leukocyte antigen [HLA]) type as the patient. Usually, the source was a brother or sister.
- When a patient needs an allogeneic transplant (stem cells from a donor), his or her doctor turns to a registry of donors—a list of people who are willing to donate to any patient in need—and of donated umbilical cord blood. The Be The Match Registry®, operated by the National Marrow Donor Program®, is the world's largest listing of volunteer donors, more than 9.5 million. Using information about the patient's HLA type, a computer program is used to scan the database of HLA types of volunteer donors.

Autologous Stem Cell Transplantation. This type of transplantation involves the use of a patient's own stem cells. The stem cells are collected from marrow or blood, then frozen. The thawed cells are returned to the patient after he or she has received intensive chemotherapy and/or radiation therapy for his or her disease. The primary purpose of an autologous transplant is to allow the patient to be given high doses of chemotherapy with or without radiation that would otherwise be too toxic to tolerate because the marrow would be severely damaged. Such high doses of treatment can sometimes overcome resistance of the disease to standard doses of chemotherapy. Autologous transplantation requires that an individual have sufficient numbers of healthy stem cells in the marrow or blood. For example, in patients with acute leukemia, remission must be achieved before the patient's marrow or blood is harvested and frozen for later use (see page 23).

This procedure is also referred to as "autologous stem cell infusion," because stem cells are not being transferred from one person to another. Since the stem cells are the recipient's own, graft-versus-host disease (GVHD) is rarely a problem. However, the patient's immune system does require time to recover after the procedure, and risk of relapse of the person's disease may be higher.

Standard Allogeneic Stem Cell Transplantation. This type of transplantation involves the use of donor stem cells. The donated stem cells can come from a related or unrelated donor. Siblings have the potential to match the patient's tissue type most closely, because the patient and the sibling donor have received their genes from the same parents. However, siblings do not always have closely matched tissue types.

The term "unrelated donor" (URD) is sometimes used to describe a donor who is not a blood relative. An unrelated donor is found by searching registries of volunteer donors for an individual who happens to be identical or very similar in tissue type to the patient. Transplant doctors can test to determine the degree of compatibility before a decision is made to use a particular donor. Compatibility is assessed by laboratory tests that identify the tissue type of both donor and recipient, called the

"human leukocyte antigen" (HLA) type. Stem cells from cord blood may also be a source for allogeneic transplants for certain patients (see page 19).

When a transplant is successful, the donor stem cells can restore normal marrow, and may provide the only long-term cure of the patient's disease. The immune system and the blood system are closely linked and cannot be separated from each other. Because of this, allogeneic transplantation means that not only the blood system but also the immune system of the donor is transferred to the recipient. As a result, these effects are possible:

- Immune rejection of the donated stem cells by the recipient (host-versus-graft effect)
- Immune reaction by the donor cells against the tissues of the recipient (graft-versus-host disease [GVHD]).

Before a standard allogeneic transplant, patients receive high doses of chemotherapy and sometimes radiation therapy. This treatment is called a "conditioning regimen" or "preparative regimen," and it destroys the cancer cells. It also suppresses the patient's immune system; therefore, the immune system is less able to attack the transplanted donor stem cells. One of the benefits of an allogeneic transplant is that the donor immune system can recognize remaining cancer cells that have survived even high doses of chemotherapy, with or without radiation, and kill them, helping to prevent disease relapse.

A critical benefit of allogeneic transplantation is the generation of a graft-versus-disease (GVD) effect that may be even more important than the very intensive therapy administered to destroy cancer cells. This effect is a result of the donor's immune system "recognizing" the patient's cancer cells and eliminating them. Unfortunately, despite appropriate tissue matching, similar donor cells may also react against the patient's normal cells and generate a potentially serious condition called "graft-versus-host disease" (GVHD). The use of autologous stem cells has neither the drawbacks of GVHD nor the advantages of a GVD effect.

The immune reaction, or GVHD, is treated by giving drugs to the recipient after the transplant to reduce the ability of the donated immune cells to attack and injure the patient's tissues (see *Graft-Versus-Host Disease*, page 31). Over time, the new immune system grown by the donor cells may develop tolerance to the host (the patient), and the immunosuppressing medications can be weaned and eventually stopped in some cases.

Reduced-Intensity Allogeneic Stem Cell Transplantation. This type of transplantation involves using less-intense conditioning treatment to prepare for the transplant as compared to standard allogeneic transplantation. With a standard allogeneic transplant, the conditioning regimen destroys most of the cancer cells. However, a reduced-intensity allogeneic transplant relies on the donor immune cells to fight the disease. Reduced-intensity allogeneic transplants (sometimes called "nonmyeloablative transplants") may be an option for certain patients who are

older, who have organ complications or who are otherwise not healthy or strong enough to undergo standard allogeneic transplantation. However, reduced-intensity allogeneic transplants do carry many of the same risks as standard allogeneic transplants, but like standard-intensity allogeneic transplants, also provide benefit via the GVD effect to help prevent disease relapse.

Research study results to date indicate that reduced-intensity allogeneic transplants are more effective as a treatment for some types and/or stages of blood cancer. Research indicates that reduced-intensity allogeneic transplants may be effective in treating certain patients with chronic myeloid leukemia (CML), acute myeloid leukemia (AML), non-Hodgkin lymphoma (NHL), chronic lymphocytic leukemia (CLL), or myelodysplastic syndromes (MDS). Your doctor will discuss whether a reduced-intensity allogeneic transplant is an option for you.

The conditioning regimen for a reduced-intensity allogeneic transplant does not destroy many cancer cells. However, it suppresses or weakens the patient's immune system so that it cannot attack the donor cells. The cells for a reduced-intensity transplant can come from a family member, an unrelated donor or, less often, a cord blood unit. The donor cells grow a new immune system and the new immune cells destroy the cancer cells.

Syngeneic Stem Cell Transplantation. This term is used to describe an allogeneic transplant when the donor and recipient are twins with identical genetic makeup and the same tissue type. With this kind of transplantation, donor cells are not rejected and the recipient's tissues are not attacked by the donor's immune cells. No treatments are needed to prevent graft rejection or GVHD. However, no beneficial GVD effect is expected either. Furthermore, as with autologous transplants, relapse of the patient's disease is more common than with other types of donors. Long-term remission is achieved in some of these patients due to the conditioning regimen effects and the infusion of normal stem cells.

Transplants continue to be improved, making transplantation a treatment option for more patients each year. The estimated number of stem cell transplants in North America in 2010, by blood cancer type, is shown in Table 1, on page 10.

Table 1. Estimated Number of Stem Cell Transplants in North America, by Blood Cancer Type, in 2010

Blood Cancer Type	Allogeneic Stem Cell Transplants	Autologous Stem Cell Transplants
Myeloma	210	5,860
Acute myeloid leukemia	2,775	155
Acute lymphocytic leukemia	1,130	0
Chronic myeloid leukemia	285	0
Non-Hodgkin lymphoma	880	2,900
Hodgkin lymphoma	190	1,020
Myelodysplastic syndromes/ Myeloproliferative neoplasms	1,030	0
Other types of leukemia	480	15
Plasma cell disorders	20	355
Total	**7,000**	**10,305**

Between 1970, when the National Marrow Donor Program® (NMDP) transplant registry began tracking data, and today, the number of blood cancer patients successfully transplanted has increased from hundreds to thousands each year. In the United States, an estimated 7,000 people had allogeneic stem cell transplants and an estimated 10,305 people had autologous stem cell transplants for blood cancers in 2010 (the most current data available).

The data presented here are preliminary and were obtained from the Statistical Center of the Center for International Blood and Marrow Transplant Research. The analysis has not been reviewed or approved by the Advisory or Scientific Committee of the CIBMTR.

Stem Cell Transplantation and Cancers of the Blood and Marrow

Transplant doctors use stem cell transplantation so they can give large doses of chemotherapy or radiation therapy to increase the chance of eliminating disease in the marrow and then restoring normal blood cell production. The infusion of stem cells from a closely matched donor, whether a sibling or unrelated donor, will begin to restore marrow function and blood cell production and allow recovery from the intensive treatment. As noted earlier, some transplants rely on immune cells from the graft (donor infusion) to suppress the underlying disease.

After several decades of research, discovery and clinical trials, allogeneic stem cell transplantation is now commonly used to successfully cure some patients who are at high risk of relapse, who do not respond fully to treatment, or who relapse after prior successful treatment. Autologous stem cells (obtained from the patient's own blood or marrow) can also be used in some circumstances.

The success of a transplant depends on appropriate timing, compared with other treatments. For patients who could benefit from a transplant, earlier treatment (rather than delayed for multiple chemotherapy or drug therapy treatments) often improves the likelihood of success and survival.

Patients with leukemia, lymphoma, myeloma, myelodysplastic syndromes or myelofibrosis whose disease does not respond to standard therapy, may be treated with very intensive chemotherapy and/or radiation therapy, which requires complementary allogeneic transplantation or autologous stem cell transplantation. The decision to use this treatment approach takes into account

- The patient's age, general health and medical condition
- The likelihood that the disease will respond to the transplant
- The availability of an HLA-matched donor or the ability to use the patient's own stem cells.

Three key questions should be answered when considering a transplant for a patient in remission:

- Does the current medical evidence indicate that stem cell transplantation will be more likely to cure the disease than other forms of therapy?
- If so, when is the appropriate time to receive the transplant?
- Is there an appropriate stem cell donor available?

Overview: Stem Cell Transplantation Options for Blood Cancers

The following information is a general summary and is not all-inclusive. Each patient has unique circumstances, so discuss all appropriate therapies with your doctor. For more detailed information, see the free LLS publications for each of the blood cancers below.

Acute lymphoblastic leukemia (ALL)

- The decision to perform a transplant for an adult who has ALL depends on the features of the leukemia, the patient's general health and the patient's age.
- For patients with high-risk ALL, an allogeneic stem cell transplant may be an option in first remission for a patient who has a suitable donor available.*
- For patients with standard-risk ALL in first remission, the choice between allogeneic transplantation and continued chemotherapy is less clear. Discuss standard and/or reduced-intensity allogeneic stem cell transplantation with your doctor to determine if either is recommended for you.
- Autologous stem cell transplantation outside of the clinical-trial setting is not commonly used to treat ALL.
- Most children with ALL (about 75 to 80 percent) do not need stem cell transplantation. A child with refractory disease (a poor response to treatment) or relapsed ALL is considered for transplantation with an allogeneic transplant.*

Acute myeloid leukemia (AML)

- Favorable-risk AML: Stem cell transplantation is generally not recommended with first complete remission.
- Intermediate-risk AML: Discuss standard and/or reduced-intensity stem cell allogeneic transplantation with your doctor to determine if either is recommended for you.
- High-risk AML: Allogeneic stem cell transplantation is generally recommended with first remission for patients who are candidates for a transplant and have a suitable allogeneic donor.* Reduced-intensity allogeneic stem cell transplantation may be recommended for older patients or patients who have certain co-morbidities.*
- Autologous stem cell transplantation may be recommended for certain patients.

Chronic lymphocytic leukemia (CLL)

- Allogeneic transplantation (usually reduced-intensity but sometimes standard) is being studied in clinical trials to treat patients who have CLL that has certain high-risk features or has relapsed after standard therapies.*

Chronic myeloid leukemia (CML)

- Oral CML therapies are generally used to treat newly diagnosed CML patients.
- In cases of advanced or refractory disease (a poor response to treatment), standard allogeneic stem cell transplantation (or reduced-intensity allogeneic stem cell transplantation) may be recommended for patients who have a suitable allogeneic donor available.*

Hodgkin lymphoma (HL)

- Autologous stem cell transplantation is used to treat HL patients whose disease relapses after initial therapy.
- Standard and reduced-intensity allogeneic stem cell transplantation are under study in clinical trials to treat HL patients who have a suitable allogeneic donor.*

Non-Hodgkin lymphoma (NHL)

- Autologous stem cell transplantation is generally used to treat patients who have relapsed or who have refractory disease; transplantation in first remission is only done in clinical trials with some exceptions—for example, in certain cases of mantle cell lymphoma.
- Allogeneic transplantation is used to treat selected patients who have NHL.
- Ask your doctor about the specific recommendations for your subtype of NHL.

Myelodysplastic syndromes (MDS)

- A standard allogeneic stem cell transplant (or a reduced-intensity allogeneic stem cell transplant for older or other selected patients) may be recommended for people who have intermediate- or high-risk MDS and a suitable allogeneic donor available.*
- Autologous stem cell transplants are used infrequently.

Myeloma

- Autologous stem cell transplantation is an important part of treatment for certain myeloma patients.
- Allogeneic stem cell transplantation is not a common treatment for myeloma patients but may be used for selected younger patients who have a suitable allogeneic donor available.*
- Reduced-intensity allogeneic stem cell transplantation is used in some cases following autologous stem cell transplantation for patients who have a suitable allogeneic donor available.*

Myeloproliferative neoplasms (MPNs)

- Myelofibrosis: A standard allogeneic stem cell transplant (or a reduced-intensity allogeneic stem cell transplant for older patients or patients who have certain comorbidities) may be recommended for certain patients who have a suitable allogeneic donor available.*
- Polycythemia vera and essential thrombocythemia: Allogeneic stem cell transplantation and reduced-intensity allogeneic stem cell transplantation are occasionally used to treat the disease.*

**Cord blood stem cells may also be a source for the graft.*

Age and Transplantation. About three-quarters of people who develop a blood cancer are more than 50 years old. In general, older individuals are more likely to

- Have complicating medical problems
- Have difficulty treating GVHD after transplantation
- Have decreased tolerance for the cumulative effects of the intensive chemotherapy and for radiation treatments needed before the transplant.

However, these are generalizations. Standard allogeneic stem cell transplantation, reduced-intensity allogeneic stem cell transplantation and autologous stem cell transplantation are procedures that can be used in older people when medically appropriate. Whether or not a patient is a candidate for transplantation is determined by medical indications (and for allogeneic stem cell transplants, the availability of a donor). There is no specific age cutoff for stem cell transplantation.

The risks of stem cell transplantation have decreased with the passing of each decade. Ongoing research is likely to continue to improve the risk-versus-benefit ratio in favor of transplantation. On the other hand, for some diseases and patients, effective new drugs and new types of therapies may lessen the potential benefits (as compared to the risk) of transplantation.

Timing of Transplantation and Tissue Typing. The points at which transplant options are considered during an individual's disease course vary. Transplantation is recommended for some patients in first remission. For others, it is recommended later on in the course of treatment for relapsed or refractory disease. This decision may depend on the response of the underlying disease to initial therapy and to other factors discussed in the previous section. If allogeneic transplantation is a consideration, it is best to have the patient's tissue typing (HLA typing) done early in the disease course. The patient's siblings should have tissue typing. If the patient does not have a sibling match, then decisions about whether to enter the patient's tissue typing into unrelated donor registries can be made. It is a good idea to do this

to determine whether suitable unrelated donor matches or cord blood matches will be available if needed. HLA tissue typing is different from the red blood cell typing used to determine blood transfusion compatibility.

Fast Facts About HLA Tissue Typing

- Almost every cell in the body displays what are called human leukocyte antigen (HLA) molecules on the cell surface. The immune system uses these molecules to verify that a given cell is part of the body and not a foreign invader.
- The HLA type can be determined by looking directly at the person's DNA, obtained from the blood or via cells from the inside of the cheek.
- The best transplant outcomes happen when the patient and the donor are HLA well-matched, meaning they share the same or almost the same HLA molecules.
- The immune reactions that occur when individuals receive a stem cell transplant are largely determined by the patient's and the donor's human leukocyte antigens; these antigens are cell surface proteins.
- In general, human cells have 46 chromosomes: pairs of chromosomes numbered from 1 to 22 plus two sex chromosomes (either XX in a female or XY in a male). A person's HLA type is governed by genes on chromosome 6.
- Testing of potential donors involves obtaining either a blood sample (usually three to four tubes of blood) or a scraping from the cheek inside the mouth (buccal scraping/swab scraping). Both samples yield enough cells for typing at protein and DNA levels.
- On average, a person has one chance in four of having the same HLA type as his or her sibling, but many patients will not have a sibling with the same tissue type (see Figure 1, page 16).
- Donor registries are in place to identify an unrelated donor who has a tissue type that matches the patient's. If you do not have a donor in your family, your doctor can contact The National Marrow Donor Program's® Be The Match Registry®, which lists more than 9.5 million potential donors and more than 165,000 cord blood units. Patients searching the Be The Match Registry also have access to additional donors through its agreements with international cooperative registries.

Inheritance and HLA Types

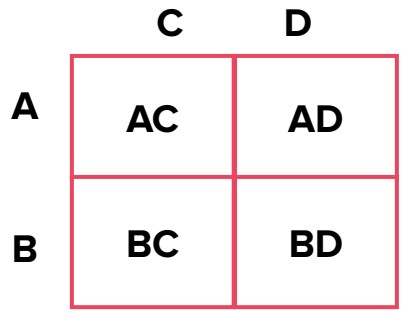


Figure 1. | Everyone inherits two sets of HLA genes: one from mother and one from father. Among four children, each will inherit a chromosome pair as shown: A or B from mother plus C or D from father. On average, in large sample sizes, a match will occur once in four chances. Within a family, there might be no match (or more than one match) among siblings.

Each parent's contribution to the HLA type is referred to as a "haplotype." The term "haploidentical" indicates that the potential donor shares half the HLA type of the potential recipient.

The HLA system is broken down into two groups of cell surface antigens: class I and class II. Class I antigens are determined by genes referred to as "A," "B" and "C." Class II antigens are determined by genes referred to as "D." A, B, C and D have many variations called "alleles" that make each individual unique. For example, one person may have A1, another A2, another A3 and so on. In families, these variations are minimized, making it more likely to find a match among siblings.

About 70 percent of patients who need an allogeneic stem cell transplant do not have a suitable donor in their family. Efforts are being made to develop methods to permit a transplant between individuals who are only partially matched. For example, the ability to transplant from parent to child would make the availability of transplantation nearly universal for childhood disorders. Children's bodies are more tolerant of deviations from ideal matching, and it is hoped that with better control of the immune reactions involved, moderately mismatched transplants may be feasible.

Pretreatment (Conditioning). High-dose chemotherapy and/or radiation therapy prior to a stem cell transplant is necessary to

- Decrease the risk that the recipient's immune cells will reject the transplanted cells in patients who are having a standard allogeneic stem cell transplant
- Eliminate any disease that might remain at the time of the transplant in patients who have blood cancer
- Eliminate the disordered lymphocytes that are attacking the patient's developing blood cells, in certain cases involving marrow failure, such as in aplastic anemia.

Patients being prepared for a reduced-intensity allogeneic stem cell transplant receive lower dosages of chemotherapy drugs and/or radiation in preparation for the transplant, compared to the dosages given to patients receiving a standard allogeneic stem cell transplant.

Stem Cell Collection for Transplantation

Overview. Stem cells for transplantation can be collected from the blood or the marrow. The patient's doctor chooses the cell source that is best for the patient, and after the preferences and consent of the donor are obtained, arrangements can be finalized.

- Donors who do not live in the same area as the transplant center can usually have samples collected for HLA typing and other blood work at a facility in their own locality and then shipped in appropriate kits to the transplant center.
- Collection of cells from sibling or related donors is usually performed at the recipient's transplant center.
- For unrelated donors, the collection is usually performed close to the donor's home, after which the blood or marrow harvest product is transported by courier to the transplant center.

The collection of peripheral blood stem cells (PBSCs) requires a nonsurgical procedure called "apheresis," which allows harvesting of blood stem cells that have been released from the marrow into the bloodstream. Normally, only a small number of stem cells circulate in the blood. When PBSCs are to be collected from a person for transplantation, injections of medication are given to move more blood-forming stem cells from the marrow into the blood. The person's blood is then removed through a needle in one arm and passed through an apheresis machine. The machine separates out all the stem cells. The remaining blood is returned through the person's other arm. Stem cells are usually back to their normal levels soon after the procedure.

The collection of stem cells from marrow is a surgical procedure. It is generally done in a hospital setting on an outpatient basis with anesthesia. Doctors use a needle to withdraw liquid marrow from the back of the pelvic bone. The marrow replaces itself completely very soon after the procedure, but because red cells are also removed, anemia may persist for a time. Before the stem cells are collected, the blood is tested for hepatitis viruses, human immunodeficiency virus (HIV) and other infectious agents. A test result that is positive for cytomegalovirus (CMV) or certain other viruses does not necessarily disqualify a person from being a donor. Also, a patient history is obtained and a physical examination is done to make sure the donation is safe.

Blood. Peripheral blood (also called "circulating blood") is currently the most common source of stem cells for transplantation. PBSCs are blood-forming stem cells released from the marrow into the blood. The use of PBSCs eliminates the need for general or spinal anesthesia when stem cells are collected from the marrow and the few days of discomfort that result at the sites where needles are inserted into the pelvic bone to obtain marrow stem cells.

Stem Cell Mobilization. Normally, the marrow releases only a small number of stem cells into the blood. To obtain enough stem cells from the peripheral blood for a transplant, a donor is usually given a white cell growth factor, such as granulocyte-colony stimulating factor (G-CSF), to encourage more blood-forming stem cells to move from the marrow into the blood. In some cases, when a patient's own stem cells are used for the transplant, the stem cells are mobilized by a combination of the chemotherapy used to treat the underlying disease and G-CSF. In patients who have myeloma or non-Hodgkin lymphoma, the drug plerixafor (Mozobil®) may be given to mobilize autologous stem cells in conjunction with filgrastim (G-CSF).

Apheresis. Once the cells are mobilized, they are collected from the blood using a process called "apheresis." For apheresis, a needle is placed in the donor's vein, usually in the arm. The blood of the donor (or the patient, in the case of an autologous transplant) is circulated through an apheresis machine, which separates the blood into four components: red cells, plasma, white cells and platelets. The white cell fraction is collected because it contains the stem cells. The rest of the blood is returned to the donor (or patient). Some donors require a central line to be placed in order to accomplish a successful stem cell collection.

The number of stem cells that must be collected depends on the patient's weight and the disease for which the transplant is being performed. A marker on the cell surface called "CD34" is used to determine the number of stem cells that have been collected. (CD is an abbreviation for "cluster designation," a term used with a number to identify a specific molecule on the surface of an immune cell.)

Stem cell collection is completed for an allogeneic transplant after one or two sessions of apheresis for the donor. In some cases, because of prior chemotherapy, autologous stem cell collections may require more than two apheresis sessions. In the unusual case where there is an inadequate autologous collection, the patient may undergo a marrow collection, or a subsequent reattempt at collection may be tried with the same or a different mobilization stimulus.

Marrow. Before a donor gives marrow, he or she needs to have a thorough physical examination, including an electrocardiogram, chest x-ray, blood chemistry evaluation and confirmation that blood cell counts are within normal limits. The donor's blood is tested to ensure that hepatitis viruses and HIV are not present. Tests are run to identify other viruses that may be present. However, positive test results (a positive CMV test result, for example) do not necessarily disqualify a donor.

Marrow donation is a surgical procedure and is performed in an operating room, using anesthesia. The transplant doctor uses a special hollow needle attached to a syringe to withdraw marrow from the top edge of the pelvic bone. This area can easily be felt under the skin of the sides and back just below the waist. The insertion of the needle through the skin and into the rim of the pelvic bone is repeated until several pints of marrow are removed. The donor usually remains in the hospital for about six to eight hours. During this time, the donor recovers from both the anesthesia and the acute pain at the needle insertion sites. The donor can typically expect to feel soreness in the lower back, which improves slowly, for a few weeks or longer. Most donors are back to their normal routine in a week. The donor's body regenerates the donated bone marrow quickly.

The amount of marrow removed from the donor is related to the size of the recipient. A large adult requires more marrow cells for the transplanted stem cells to engraft than a small child does. The harvested marrow is passed through a series of filters to remove fragments of bone or tissue and then placed in a plastic bag from which it can be infused into the recipient's vein. It is usually administered to the recipient within a few hours and, in most cases, within less than 24 hours. If necessary, the harvested marrow cells can be frozen and stored for later use. The marrow can be frozen for years and remain suitable for stem cell transplantation. Freezing is commonplace in anticipation of autologous stem cell infusion. In this circumstance, the patient's own stem cells from blood or marrow are collected during a period of disease remission following treatment. The stem cells are thawed and then returned to the patient after the intensive conditioning treatment has been given.

Cord Blood. The blood in the umbilical cord and placenta contains stem cells. This blood can be collected after the baby is born; the collected blood is called a "cord blood unit." During delivery, the focus is on the mother and baby. After the baby is delivered, the umbilical cord is clamped. The blood from the umbilical cord and placenta is collected before or after the placenta is delivered, depending upon the procedure at the hospital. Blood is collected into a sterile bag; this bag of blood is the cord blood unit. The collected blood is given an identification number and stored temporarily. The cord blood unit is transported to a cord blood bank for testing, freezing and long-term storage.

Testing procedures include HLA typing to determine the level of matching to potential recipients, cell counts and testing for infectious agents such as the HIV, CMV and hepatitis viruses. The cord blood unit is checked to make sure it has enough blood-forming cells for a transplant. If there are too few cells, the cord blood unit may be used for research to improve the transplantation process for future patients, or it may be discarded. Next, the blood is frozen and stored at a very low temperature, usually in liquid nitrogen, for future use. When needed for a transplant, the cord blood unit can be shipped, often within a few days, to the transplant center, where it is thawed and infused into the patient. Some mothers elect to have their baby's cord blood stored privately. Such cord blood units are not available through the registries for general use.

The number of cells required to give a transplant patient the best chance for engraftment and for surviving the transplant is based on his or her weight. A cord blood unit needs to have a sufficient number of stem cells based on the recipient's size. Due to the smaller number of stem cells in the cord blood unit, cord blood stem cell transplants engraft more slowly than stem cells from marrow or peripheral blood. Until engraftment occurs, patients are at risk of developing life-threatening infections.

Cord blood transplants may require a lower level of matching between the donor and recipient. When compared to other transplants, these transplants using the less mature stem cells from cord blood seem to be associated with a decreased risk of GVHD. Also, research is under way to improve the yield of cord blood stem cells and to examine the use of more than one cord blood unit per transplant to see if this improves the time to engraftment. See the free LLS publication *Cord Blood Stem Cell Transplantation* for more information.

T-Lymphocyte Depletion. T lymphocytes in a donor's marrow or blood can cause GVHD. On the other hand, T lymphocytes are also beneficial. They help the donated stem cells take hold (engraft) and grow in the recipient's marrow. In some cases, T lymphocytes attack blood cancer cells, enhancing the results of other treatment. This is the graft-versus-tumor (GVT) effect and is seen mostly in the myeloid (myelogenous) leukemias. The attack on the remaining blood cancer cells makes it less likely that the disease will return after transplantation. A procedure called "T-lymphocyte depletion" can be utilized in certain circumstances. With this procedure, the stem cells collected for the transplant are treated with agents to decrease the number of T lymphocytes that would be infused with the stem cells. The aim of using this approach is to reduce the incidence and severity of GVHD. However, T-lymphocyte depletion may result in increased rates of graft rejection, decreased GVT effect and slower immune recovery. For these reasons, T lymphocytes are depleted from the stem cell collection only in certain circumstances, and transplant doctors must be careful about how many T lymphocytes are removed when this procedure is used.

Stem Cell Selection. There are specific features on the outer coat of stem cells that permit them to be removed selectively from a mixture of cells. In some cases, the collected stem cells may be depleted of most T lymphocytes, as described in the previous section. Alternatively, a procedure called "stem cell selection" may be used before the stem cells are administered to the recipient. This procedure results in a marked decrease in the number of T lymphocytes that the patient receives. This selection process results in a cell population that is enriched in stem cells and has many fewer other cells, including T lymphocytes. The aim of reducing the number of T lymphocytes is to reduce the frequency or severity of GVHD. This selection procedure is not routinely used but may be used in certain clinical trials.

Transfusing the Stem Cells. The infusion of stem cells into the recipient's vein is similar to a blood transfusion. However, stem cell infusion is given through a central line into a large blood vessel. The same type of administration is used for

marrow, PBSCs or cord blood stem cells. (Stem cell infusion is also referred to as "stem cell transfusion.")

Most central lines are positioned on the chest wall. Placement is usually done with local anesthesia. To place the central line, a small incision is made where the catheter (tubing) enters the vein, and the opposite end of the catheter is passed under the skin and exits at a second small incision made at a distance from the first incision. This distance helps prevent infection. There may be a few stitches at one or both sites until the areas have healed. Small, clear dressings are changed frequently to prevent infection.

The transfusion process consists of the following measures:

- The donor stem cells are collected in a plastic blood transfusion bag. If stem cells are from marrow, special filters are used to separate bone fragments, fatty particles and large clusters of cells from the collected stem cells before the product is placed into the transfusion bag. This is done in the operating room. The product is then sent to a blood bank or cell-processing laboratory where
  - The number of cells is determined
  - Either the red cells or the plasma (the fluid surrounding the cells) may need to be removed if the donor and recipient do not share the same red blood cell type.
- Infusing the stem cells usually takes several hours. Patients are checked frequently for signs of fever, chills, hives, a drop in blood pressure or shortness of breath. Side effects occasionally occur; these are treated and the infusion is completed. Often, patients experience no side effects from the infusion.

Reactions from the cryopreservative in the stem cell collection that has been frozen and thawed may also occur in patients receiving this treatment. Side effects may include headache, nausea, flushing and shortness of breath. These problems can usually be managed and the infusion completed.

Autologous Stem Cell Transplantation

Autologous stem cells are used to restore blood cell production after intensive radiation and/or chemotherapy in the treatment of pediatric and adult patients, thereby making treatment with high-dose chemotherapy and radiation therapy possible. Autologous stem cell transplantation is used mainly to treat people who have a blood cancer diagnosis, but may be used to treat patients who have some other types of cancer.

Fast Facts About Autologous Transplantation

- The infusion of autologous stem cells does not carry the risk of either graft rejection or graft-versus-host disease (GVHD).
- Autotransplantation does not require immunosuppressive treatment. However, the patient receives intensive cytotoxic therapy to kill residual blood cancer cells (see Figure 2, page 23).
- The principal concerns with autologous transplantation are that
  - The number of collected stem cells (called an "autograft") returned to the patient be enough for full engraftment
  - Any tumor cells in the autograft are not enough to reestablish the disease in the patient. (There is a possibility that the patient's blood cancer cells may contaminate an autograft, even when obtained from a patient in remission. However, purging techniques used in an attempt to eliminate any remaining malignant cells have not improved outcomes and are no longer performed, except in clinical trials.)
- The main adverse effects of autologous transplantation result from the high-intensity conditioning therapy used to destroy remaining cancer cells.
  - Markedly decreased blood counts may lead to
    - –Infection
    - –The need for transfusions of red cells (for anemia) or platelets (to prevent or treat hemorrhage).
- Certain conditioning drugs can produce specific complications, especially interstitial pneumonia, which may be the result of infection or damage from intensive therapy.
- Oral mucositis (painful oral ulcers) may develop; rarely, these can prevent fluids or solids from being taken by mouth. When needed, agents such as the epidermal (skin type cells) growth factor palifermin (Kepivance®), given intravenously, can be used to prevent or minimize the effects of oral mucositis. Other measures can also be used to prevent and treat this complication.

Autologous Transplantation

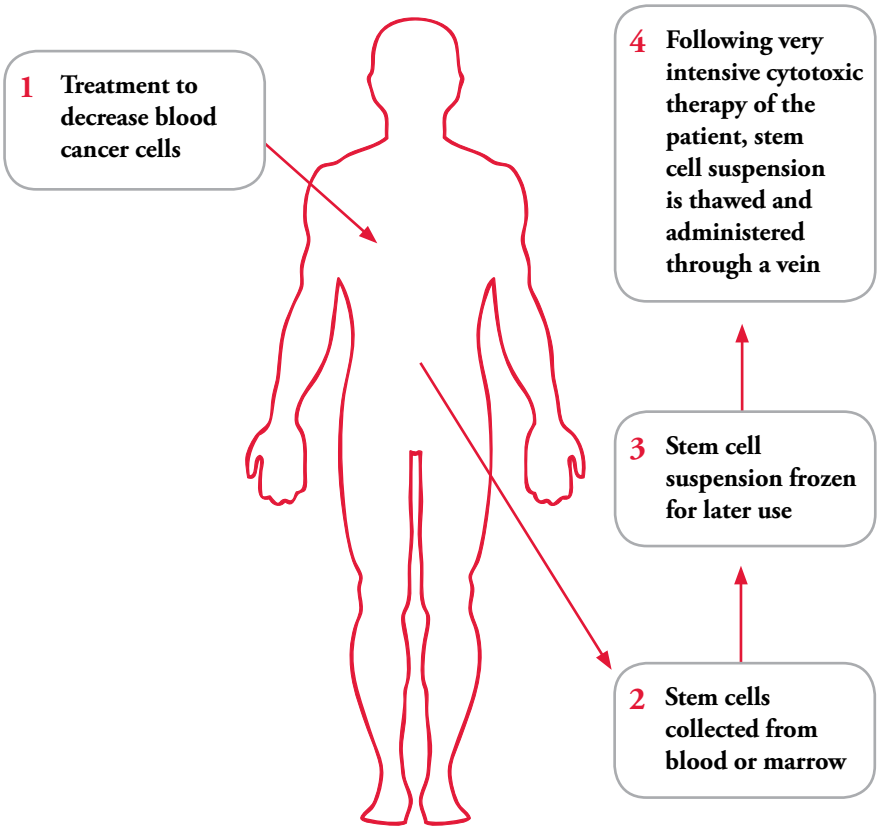


Figure 2. | This diagram explains the steps involved in autologous stem cell transplantation. 1) The patient is treated to control the disease and to markedly decrease the number of cancer cells in marrow and blood. 2) The stem cells from blood or marrow are then harvested. If blood is used as the source of stem cells, the patient is treated with a stem cell mobilizer after chemotherapy, which draws stem cells out of the marrow and into the blood. If the marrow is the source of stem cells, the marrow is removed under sterile conditions in the operating room while the patient is anesthetized. 3) The cells are mixed with a cryoprotective agent so that they can be frozen and later thawed without injury. 4) At a later time, when the patient is treated intensively with chemotherapy and/or total body radiation that destroys the marrow function, the frozen stem cell collection is thawed and infused into the patient so that blood cell production can be restored.

Standard and Reduced-Intensity Allogeneic Stem Cell Transplantation

"Standard allogeneic stem cell transplantation" is the term used in this booklet to indicate that the patient receives a high-dose conditioning regimen prior to transplantation to severely or completely impair his or her ability to make stem cells (see Figure 3, page 26). High-dose conditioning regimens are used for a large percentage of patients undergoing allogeneic stem cell transplantation. These high-dose regimens are particularly useful in conditioning patients with diseases where there is a need for strong aggressive anticancer agents along with the immunologic effects of the graft.

Fast Facts About Standard Allogeneic Transplantation

- Two processes are necessary for a successful standard allogeneic stem cell transplant:
  - Suppression of the recipient's immune system before the transplant
  - Suppression of the donor immune cells after the transplant.
- Prior to transplantation, the patient receives a conditioning regimen that
  - Treats the remaining cancer cells intensively to make a recurrence of the cancer less likely
  - Inactivates the patient's immune system to minimize the chance of stem cell graft rejection
  - Enables donor immune cells to engraft and exert their potent antitumor effect.
- The degree of difference in tissue type between donor and recipient is the main determinant of
  - The intensity of host-versus-graft (HVG) effect (when the patient's cells reject the donor stem cells)
  - Graft-versus-host disease (GVHD) (when the donor stem cells attack the patient's cells).
- HVG effect and GVHD
  - Do not occur if the recipient and the donor are identical twins
  - May occur if the recipient and the donor are siblings who are not identical twins, even if they are matched by tissue typing.

Standard Allogeneic Stem Cell Transplantation Conditioning Regimens. A number of different high-dose conditioning regimens can be used, depending on the type of blood cancer and other factors. The treatment may consist of chemotherapy drugs alone (for example, busulfan [Myleran®] and cyclophosphamide [Cytoxan®]) or chemotherapy given with total body radiation. Certain conditioning regimens may have unique side effects, and members of the transplant team will discuss these with the patient before beginning the conditioning therapy.

Radiation therapy is administered in several divided daily doses. This technique is referred to as "fractionation of the dose." Fractionation minimizes side effects such as lung injury, nausea and vomiting (see Table 2, page 28). The drugs and radiation therapy are given throughout the week before a transplant. The number of treatment days and the sequence of administration depend on the specific conditioning regimen. The days prior to the transplant are labeled day minus 6, minus 5, and so on; transplantation (donor stem cell infusion) is day zero; the day after the transplant starts with plus 1, plus 2, and so forth.

The Immediate Posttransplant Period. Patients may experience side effects during the days they are receiving the high-dose conditioning radiation or chemotherapy. Often by the second or third day after an allogeneic stem cell infusion, the decrease in marrow function begins to have its effects. The allogeneic stem cell transplant patient is usually kept in a protected environment to minimize contact with infectious agents (see *Infection* on page 30), but in some centers, transplants can be accomplished on an outpatient basis.

Generally within two to four weeks after the transplant, the engraftment of donated cells is apparent from the appearance of normal white cells in the patient's blood. The patient receives periodic transfusions of red cells and platelets until marrow function is restored by the transplanted stem cells. Careful monitoring of the patient by physical examinations, blood chemistries, imaging studies and other tests is done to ensure that major organs such as the heart, lungs, kidneys and liver are functioning normally.

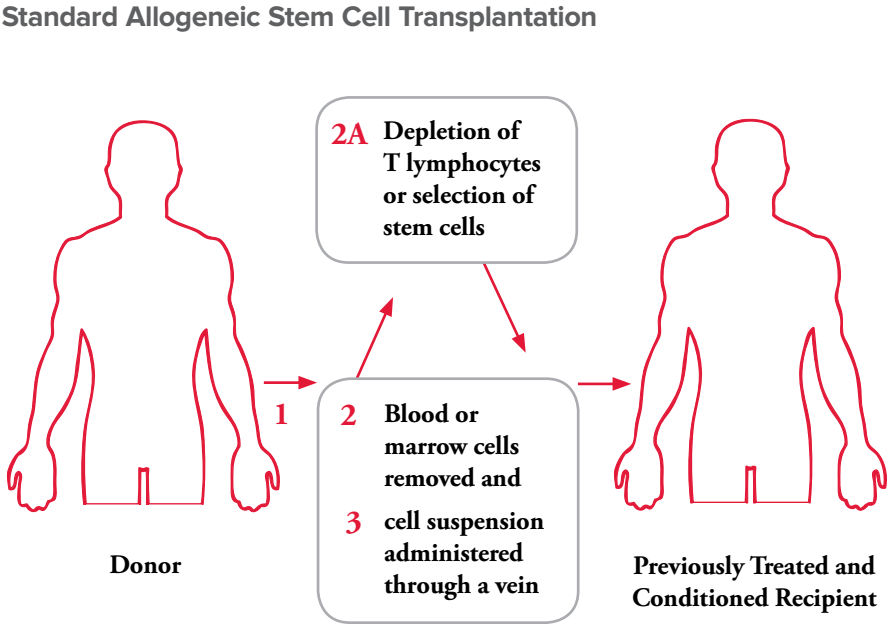


Figure 3. | A matched related or unrelated donor is identified. 1) When peripheral blood stem cells are used as the source of stem cells for the transplant, the donor is treated with a stem cell mobilizer to draw stem cells out of the marrow into the blood. The stem cells from blood are recovered by apheresis. When marrow is the source of stem cells, the donor is anesthetized and the cells are harvested in an operating room. The marrow stem cell collection is filtered and placed in a plastic bag. 2) and 3) The stem cell collection is administered through a vein to the recipient, who has been treated intensively with total body irradiation and/or chemotherapy. 2A) In some cases, the stem cell collection may be depleted of most T lymphocytes. Alternatively, stem cell selection may be employed, which results in a marked decrease in the number of T lymphocytes. Then the stem cells are administered to the recipient.

Patients who have an allogeneic transplant require drugs to prevent GVHD, and most will require red cell and platelet transfusions. Periods of duodenal tube or intravenous feeding, called "hyperalimentation," may be needed for some patients to ensure adequate nutrition intake in the presence of poor appetite, mouth sores, and diarrhea.

Reduced-Intensity Transplantation Basics

Allogeneic stem cell transplants for older patients, or patients with overall poor health, have been relatively uncommon. This is because the pre-transplant conditioning therapy is generally not well tolerated by such patients, especially those with poorly functioning internal organs. Sufficient numbers of reduced-intensity allogeneic stem cell transplants have been performed to conclude that this may be appropriate treatment for certain older, sicker or other selected patients.

Fast Facts About Reduced-Intensity Allogeneic Transplantation

- Transplant doctors have been developing reduced-intensity conditioning regimens that may help selected patients with suitable donors, including cord blood units, up to the seventh and eighth decades of life who have
  - Less rapidly progressive blood cancers
  - Certain infections or additional serious medical conditions such that a standard allogeneic transplant would not be indicated.
- Reduced-intensity stem cell transplantation does not completely destroy the patient's diseased marrow and relies on donor immune cells to fight the patient's disease.
- Conditioning therapy for reduced-intensity stem cell transplantation varies among transplant centers. It ranges from very-low-intensity treatments to those only somewhat milder than high-dose conditioning regimens.
- Some reduced-intensity stem cell transplants are of intermediate intensity and may be used when a standard allogeneic transplant could not be tolerated but a reduced-intensity transplant would not be sufficient treatment.
- Graft-versus-host disease (GVHD) is an important and potentially disabling side effect of both standard and reduced-intensity allogeneic stem cell transplantation.

The effectiveness of reduced-intensity transplants depends on the graft-versus-tumor (GVT) effect, in which the recipient's new immune system (originating from the donated stem cells) may destroy the bulk of remaining cancer cells. The procedure uses less intense doses of either radiation or chemotherapy than a full-intensity transplant to condition the patient. Potent immune therapy is given to suppress the recipient's T lymphocytes to avoid rejection of the donor stem cells. The goal is to have the donor stem cells take up residence in the recipient's marrow and produce lymphocytes (immune cells) that attack the patient's blood cancer cells. When the immune cells made from the donor attack and suppress the remaining cancer cells in the recipient, the transplant is considered successful. The GVT effect underlying both standard allogeneic and reduced-intensity allogeneic stem cell transplantation is strongest in patients being treated for chronic myeloid leukemia (CML). Patients with other malignancies also benefit from GVT but to lesser degrees.

Reduced-intensity allogeneic stem cell transplants are usually performed with peripheral blood stem cell grafts, but stem cells from marrow or cord blood can be used. In some instances where the donor's immune system does not completely replace that of the recipient (a state called "mixed chimerism"), extra boosts of donor immune cells (lymphocytes) can be infused to improve the engraftment and

possibly the immune system's antitumor effects. These infusions are called "DLI" (donor leukocyte infusion) therapy.

Many centers are working to answer questions about the risks and benefits of reduced-intensity transplants. To locate transplant centers performing reduced-intensity transplantation,

- Speak to your doctor
- Contact our LLS Information Specialists at (800) 955-4572 or access the LLS website at www.LLS.org
- Search for the locations of clinical trials using an LLS-sponsored online search tool at www.LLS.org/clinicaltrials.
- Visit the Be The Match® website, www.BeTheMatch.org, for a listing of transplant centers
- Contact the National Cancer Institute at 800-4-CANCER (800-422-6237) or access the NCI website at www.cancer.gov.

Side Effects of Conditioning Treatment for Stem Cell Transplantation

The conditioning treatment given prior to allogeneic or autologous transplantation can affect any body system that depends on replacement by stem cells (see Table 2, below) or that may be directly affected by chemotherapy or radiation. Some of these effects manifest quickly; others may not appear for years.

Table 2. Some Side Effects of Conditioning Treatment

Cataracts	Loss of blood cell formation
Congestive heart failure	Mucositis
Diarrhea	Nausea and vomiting
Growth retardation	Occlusion (blockage) of veins in liver
Hair loss	Pneumonitis (pneumonia)
Infertility	Premature menopause

For information about conditioning therapy for a reduced-intensity allogeneic stem cell transplant, speak to your doctor to see how these side effects may apply.

Effects of Cell-Damaging Chemotherapy and Radiation Therapy. The following areas are especially sensitive to cytotoxic drugs and radiation therapy.

Gastrointestinal Tract. Ulcers and other gastrointestinal tract side effects are common. These include mouth sores (oral mucositis), nausea, diarrhea, intestinal cramps and rectal or anal ulceration. Several strategies, including treatment with a skin-cell growth factor, palifermin (Kepivance®), may be used to minimize the severity of oral mucositis. Palifermin stimulates the cells that line the mouth and gastrointestinal tract to grow and develop.

Hair. Hair loss occurs with many conditioning regimens. It is generally temporary, and hair growth resumes when drug dosages are decreased or the drugs are discontinued.

Heart. Some conditioning therapies can affect the heart. The effect may be temporary but can sometimes be permanent. Prior to transplantation, patients have tests, such as an echocardiogram (ECHO), to see how well the heart is working.

Lungs. This part of the body is sensitive to the conditioning regimen, especially with total body radiation along with chemotherapy. A reaction called "interstitial pneumonitis" (pneumonia) can occur. This side effect is caused by a tissue reaction and does not mean that an infection is present. However, it can be very severe and prevent the efficient exchange of oxygen in the lungs. This complication is treated with drugs. It may occur at any time—from a few days after high-dose chemotherapy to several months after treatment—and may even occur after a patient has returned home from a transplant center. It is important for a patient who experiences shortness of breath or a new cough after an allogeneic transplant to bring this to the immediate attention of his or her doctor.

Skin. Rashes may develop. Skin effects are evaluated and treated to help make patients more comfortable and to prevent serious complications.

Blood Vessels. Leaky blood vessels may result from the accumulated injury caused by chemotherapy and radiation therapy. (Chemicals released as a result of the immune reactions to donor cells also contribute to this effect by damaging vessel walls.) Fluid escapes from the vessels and accumulates in the tissues (edema). In the lungs, fluid accumulation may cause congestion, poor exchange of oxygen and shortness of breath. Agents such as corticosteroids, which decrease inflammation, are sometimes used to manage this complication.

Liver. The blood vessels that lead into and pass through the liver are prone to blockage after transplantation. This serious side effect is called "veno-occlusive disease" (VOD). It is brought about by toxic changes in the liver due to chemotherapy and radiation therapy. Signs include jaundice (yellowing of the skin and eyes) and an accumulation of fluid in the abdomen and elsewhere. Sometimes toxins normally removed by the liver can accumulate, leading to mental confusion

and sleepiness. Treatment of VOD may include red blood cell transfusions, diuretics and drug therapy, such as the agent defibrotide, which is being examined in clinical trials for its potential benefit in this setting.

Infection. Intensive treatment is usually required to suppress immune function when donor cells are transplanted and to kill tumor cells prior to the transplant. The resulting suppression of white cells that normally prevent or combat infections leads to a high risk of infection. Infections by bacteria, fungi, viruses or other parasites are likely. These organisms are present most often on the skin and in the mouth or the lower bowel. They are also found in uncooked food (for example, leafy green salads) and in the air.

When blood cell and immune cell levels are normal, and when the skin and lining of the mouth and bowel are intact, the body easily fends off such microbes. These normal defenses are lost in transplant patients. For this reason, antibiotics and other antimicrobial drugs are sometimes administered to patients in anticipation of the development of infection. The drugs are usually continued until the white cells reappear in the blood in sufficient numbers to make infections unlikely. The term "opportunistic infection" applies to infections caused by bacterial, fungal and viral agents that rarely cause disease in healthy persons but cause infection in persons with severe immunodeficiency. Many precautions are taken to minimize the risk of infection. Measures to combat infection include the use of a single room with filtered air, control of contact with visitors, use of masks and meticulous hand washing by staff and visitors who enter the patient's room. Central-line sites must be kept clean. Patients are usually advised to eliminate certain foods that may carry microorganisms, such as raw eggs or raw seafood. Fruits that are washed or peeled are usually allowed, but recommendations vary from center to center.

By implementing several of these measures to prevent or manage infection, it helps to isolate the patient for the month, or sometimes longer, that it takes for the donor stem cells to begin forming enough blood and immune cells to replenish the body's immune system.

Graft-Versus-Host Disease

Graft-versus-host disease (GVHD) is a side effect that occurs in many allogeneic and reduced-intensity allogeneic transplant patients. With GVHD, the transplanted donor immune cells attack the patient's body, causing various effects (see Table 3, below). Medications are given to help prevent GVHD. These are usually started one to two days before the stem cell infusion. Multiple agents have been used to help prevent GVHD. Common regimens include cyclosporine and methotrexate; tacrolimus (Prograf®) and methotrexate; and tacrolimus and mycophenolate mofetil (CellCept®), among others. A combination of tacrolimus and sirolimus (Rapamune®) has been reported to be effective for the prevention of GVHD. All of these regimens suppress the immune system, and patients may need to continue to take such medications for many months after transplantation.

GVHD may be acute or chronic. Its severity ranges from a mild condition to one that is life-threatening. The severity of GVHD depends on the differences in tissue type between patient and donor.

Table 3. Some Effects of GVHD

Skin changes	Liver injury
Gastrointestinal tract malfunction	Other organ system impairment

GVHD results when the donor's immune cells, especially the T lymphocytes, sense that the host cells are different from themselves. In the case of stem cell transplantation, the donor cells monitor the recipient's cells for differences and attack them if they find significant variations. The differences may involve cell surface proteins that are not measured by HLA typing, or there may be subtle differences in HLA type that permit transplantation but cause the reaction. Except in the case of identical twins, some incompatibility will exist even though HLA testing indicates enough similarity to permit a successful transplant.

Acute GVHD. Acute GVHD can occur soon after the transplanted cells begin to appear in the recipient. Typically, acute GVHD will manifest in the first 100 days but may appear later. The first signs are usually

- A rash, with burning and redness of the skin. This may erupt on the patient's palms or the soles of the feet but often involves the trunk and other extremities as well. The skin may blister, and in severe cases of GVHD the exposed surface of the skin may flake off.
- Nausea, vomiting, abdominal cramps and loss of appetite, indicating involvement of the gastrointestinal tract. Diarrhea is common.
- Jaundice, which may indicate that GVHD has injured the liver. Abnormalities of liver function would be noticed on blood test results.

Acute GVHD may be mild, moderate or severe. It may be a life-threatening condition if its manifestations are difficult to control. It is usually diagnosed by biopsy of one of the involved organs, and it is given a grade from I (mildest) to IV (most severe). Older patients are more likely to develop acute GVHD than younger patients.

Chronic GVHD. Chronic GVHD usually occurs after the third month posttransplant, but may not develop for a year or more after the transplant. Older patients are more likely to develop chronic GVHD than younger patients. It is also more likely to occur in patients who previously have had acute GVHD, but it may appear without prior acute GVHD.

Most patients with chronic GVHD experience skin problems. A rash and itching may occur first. The skin may become scaly. If the reaction is severe, patches of skin pigmentation may be lost or the patient's skin color may deepen and the texture become very hard. The skin may heal by scarring, and the motion of nearby joints, such as the fingers, may be restricted. Hair loss may accompany the skin injury.

The drying and scarring effects of the attack by the donor immune cells can affect the inside of the mouth and the esophagus (the tubular passage that extends from the throat to the stomach). It may become excessively dry and damaged, and ulcers may result. The tendency to drying may lead to loss of tear formation and general eye redness and irritation; dryness of the vagina and other surfaces may also occur. The lungs may also show effects of drying and scarring. Liver injury may result in failure of liver function and the diminished flow of bile. In severe cases, the bile may back up into the blood and cause jaundice. In other cases, these problems may not be overt, but they can be detected by blood chemistry measurements. Chronic GVHD can be mild (with later improvement), or more severe, persistent and incapacitating.

Treatment for GVHD. Several drugs are used to prevent or minimize GVHD. The development of new drugs to treat GVHD, combined with early detection and advances in understanding the disease, have resulted in significant reductions in serious or fatal outcomes from GVHD. Successful treatments for both acute and chronic GVHD have been developed, but GVHD does not always respond to these treatments and can still result in fatal outcomes in some cases. Many deaths related to GVHD occur as a consequence of infections that develop in patients with suppressed immune systems.

Advances in transplantation techniques, such as more precise HLA matching, treating patients with immunosuppressive drugs, depletion of T lymphocytes from the donor graft and using umbilical cord blood as the source of donor cells have helped to reduce patients' risk of developing acute GVHD.

If acute GVHD does develop after transplantation, glucocorticoids such as methylprednisolone or prednisone are administered. New drugs and strategies

that are available now or in clinical trials can supplement standard treatment. They include but are not limited to

- Antithymocyte globulin (rabbit ATG; Thymoglobulin®)
- Denileukin diftitox (Ontak®)
- Monoclonal antibodies, such as infliximab (Remicade®); or, more rarely, alemtuzumab (Campath®)
- Mycophenolate mofetil (CellCept®)
- Sirolimus (Rapamune®)
- Tacrolimus (Prograf®)
- Oral nonabsorbable corticosteroids such as budesonide or beclomethasone dipropionate
- Intra-arterial corticosteroids
- Pentostatin (Nipent®)
- Extracorporeal photopheresis (procedure)
- Infusions of mesenchymal stem cells (experimental only at this time).

Primary therapy for chronic GVHD is administration of corticosteroids. Cyclosporine may be combined with prednisone. Clinical trials investigating steroid-refractory GVHD have reported some success for the following treatments, among others:

- Etanercept (Enbrel®)
- Extracorporeal photopheresis (procedure)
- Infliximab (Remicade®)
- Mycophenolate mofetil (CellCept®)
- Pentostatin (Nipent®)
- Rituximab (Rituxan®; role still being investigated)
- Tacrolimus (Prograf®)
- Thalidomide (Thalomid®)
- Imatinib mesylate (Gleevec®) for some skin changes.

Drug dosages depend on the severity of the graft-versus-host reaction and on kidney and liver functions. Supportive care measures for the skin, eyes, oral cavity, vaginal mucosa and lungs are also important, as is attention to nutrition. One of the most important aspects of chronic GVHD treatment is surveillance for and

treatment of any infections that may develop in this condition, where the immune system is suppressed by both the disease itself and its treatments. If GVHD stabilizes or improves, the dosages of medications for GVHD may sometimes be tapered, and then, eventually, the drugs may be discontinued.

Usually, after a year or so, new T lymphocytes are formed from the engrafted donor cells. The newly formed lymphocytes do not attack the recipient's cells, and immunosuppressive therapy can be stopped. The patient's immune system can work efficiently to protect against infections, and risk of infection begins to approach that of a healthy person. This "state of tolerance" between the donor immune cells and the recipient's cells, which is anticipated to occur over time, is important for the long-term success of the transplant.

Posttransplantation

Autologous or allogeneic stem cell transplantation, or a portion of an either type, may be done in an outpatient or inpatient setting. On average, patients who are treated on an inpatient basis recover sufficiently to leave the hospital in three to five weeks posttransplant. (The length of stay varies, so patients are advised to check with their doctors.) Before discharge, both the doctor and patient should feel comfortable that there is no remaining need for hospitalization. The recovery rate of blood cell counts and the severity of other associated complications, especially graft-versus-host disease (GVHD), vary from patient to patient. A patient is ready for discharge when

- The patient's marrow is producing a sufficient number of healthy red cells, white cells and platelets
- There are no severe treatment complications
- The patient has a sense of well-being (as a result of restored blood cell counts)
- Mouth sores and diarrhea lessen or disappear
- Appetite improves; it is important that patients be able to eat and drink to get sufficient fluid and nourishment before they are discharged from the hospital
- The patient does not have fever and is not vomiting.

Many patients will have a central line in place. Hospital or clinic staff will show patients or family members how to clean and care for the central line at home. Also, home care agencies can provide help with catheter care at home to help prevent infection.

Some allogeneic or autologous stem cell transplant patients may require posttransplant hospitalization for a variety of reasons. A return to the hospital may be for a problem such as infection, management of dehydration or management of GVHD.

Aftercare. In general, there is a shorter recovery period after autologous stem cell transplantation than after allogeneic stem cell transplantation. Some of the complications and restrictions described in this section are identified as applying mainly to allogeneic stem cell transplant patients.

After the transplant, patients and families are instructed in at-home care needs. They learn the signs, such as fever, pain or diarrhea, that should prompt a call to their healthcare provider. Home visits by nurses or doctors and patient visits to the outpatient clinic are important for follow-up and adjustment of activities and medications. Initially, visits may be frequent, and allogeneic transplant patients may need follow-up visits several times per week. If all is going as anticipated, the central line can be removed and the frequency of follow-up visits can gradually be decreased. Many autologous transplant patients can be followed by their referring oncologist within a short time posttransplant.

It often takes at least 6 to 12 months to recover nearly normal blood cell levels and immune cell function in a patient who receives an allogeneic transplant. Below are some important points regarding posttransplant follow-up.

- Patients should discuss their risk of infection and any recommended precautions and prophylactic antibiotics with their doctors.
- Patients may be advised to avoid contact with children who have had recent immunization with live viruses.
- The lenses of the eyes of patients treated with total body radiation during conditioning would have been irradiated, and there is the possibility that cataracts may develop. This may not occur until several years after the transplant.
- Irradiation of the gonads may lead to infertility. Hormone replacement is usually not necessary for men. For women, estrogen and progesterone replacement therapy may be needed. Fertility may persist in some patients, so when pregnancy is not desired, contraceptive measures are important.
- Children may have a slowed growth rate and may require growth hormone treatment and replacement of other hormones. In young patients, puberty may be delayed and hormonal therapy required.
- Radiation may decrease thyroid function, so thyroid hormone may need to be administered orally.
- The severity of chronic GVHD is the major determinant of the patient's quality of life. This immune reaction can result in serious complications, including troublesome infections. Treatment for severe GVHD can also cause complications.

Long-term follow-up care is important after both autologous and allogeneic transplantation. If a patient is unable to return to the transplant center for yearly follow-up visits, it is important that his or her local oncologist be aware of all the recommendations for follow-up related to various organ systems. In addition to the

items mentioned in this section, attention to bone health for those patients who require corticosteroid therapy is important. New vaccinations to boost immunity to various infectious agents are usually administered after one year, and the patient's transplant doctor can provide a schedule for these. Observation for secondary malignancies, dental caries and dry eyes or cataracts is also important.

See the free LLS fact sheets *Fertility, Long-term and Late Effects of Treatment in Childhood Leukemia or Lymphoma Facts* and *Long-term and Late Effects of Treatment in Adults Facts* for more information about treatment effects and follow-up care.

Posttransplant care guidelines have been developed for patients (see Resources) and doctors (see References).

Clinical Trials

New approaches to treatment in clinical trials, many of which are being supported by LLS research programs, hold the promise of improving the rate of remission and the cure rate for patients with blood cancers.

LLS is funding research in leukemia-peptide vaccines to find out if they are safe and capable of generating an effective immune response among healthy bone marrow transplant (BMT) donors and recipients with leukemia; to improve immune function and control tumor cells to maximize the potential of immunotherapy; to examine whether the investigational drug roscovitine might affect recovery of the immune system after allogeneic stem cell transplantation and, if so, to develop a clinical trial to use roscovitine to prevent GVHD in humans; to clarify key genetic/functional features of optimal transplant donors who exert immunity against leukemia—studies that will lead to the development of an entirely new class of immuno-modulatory drugs that reduce GVHD and make BMT safer.

Clinical Trials. Every new drug or treatment regimen goes through a series of studies called "clinical trials" before it becomes part of standard therapy. Clinical trials are carefully designed and rigorously reviewed by expert clinicians and researchers to ensure as much safety and scientific accuracy as possible. Participation in a carefully conducted clinical trial may be the "best available" therapy. Patient participation in clinical trials in the past has resulted in the therapies we have today.

LLS Information Specialists, at (800) 955-4572, can offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. Information Specialists will conduct individualized clinical-trial searches for patients, family members and healthcare professionals. This service is also available at www.LLS.org/clinicaltrials.

Research Approaches. A number of approaches are under study in clinical trials on stem cell transplantation treatment. Studies are under way to find a means to shorten immune system recovery for recipients of partially matched (haploidentical)

donor cells. These may involve donor vaccinations and adding back T lymphocytes that are specific for certain infections after the transplanted cells have engrafted.

We encourage you to contact our Information Specialists and visit www.LLS.org for more information about specific treatments under study in clinical trials.

Normal Blood and Marrow

Blood is composed of plasma and cells suspended in plasma. Plasma is largely made up of water in which many chemicals are dissolved. These chemicals include

- Proteins
  - Albumin, the most common protein in blood
  - Blood-clotting proteins, made by the liver
  - Erythropoietin, a protein made by the kidneys that stimulates red cell production
  - Immunoglobulins, antibodies made by plasma cells in response to infections including those we develop from our vaccinations (such as poliovirus antibodies, which are made by normal plasma cells in the bone marrow)
- Hormones (such as thyroid hormone and cortisol)
- Minerals (such as iron and magnesium)
- Vitamins (such as folate and vitamin B_{12})
- Electrolytes (such as calcium, potassium and sodium).

The cells suspended in plasma include red cells, platelets and white cells (neutrophils, monocytes, eosinophils, basophils and lymphocytes).

- The red cells make up a little less than half the volume of the blood. They are filled with hemoglobin, the protein that picks up oxygen in the lungs and delivers it to the cells all around the body; hemoglobin then picks up carbon dioxide from the body's cells and delivers it back to the lungs, where it is discharged when we exhale.
- The platelets are small cells (one-tenth the size of red cells) that help stop bleeding at the site of an injury in the body. For example, when a person has a cut, the vessels that carry blood are torn open. Platelets stick to the torn surface of the vessel, clump together and plug up the bleeding site with the help of blood-clotting proteins such as fibrin and electrolytes such as calcium. Later, a firm clot forms. The vessel wall then heals at the site of the clot and returns to its normal state.
- The neutrophils and monocytes are white cells known as "phagocytes" (eating cells) because they can ingest bacteria or fungi and kill them. Unlike the red cells

and platelets, the monocytes can leave the blood and enter the tissues, where they can attack invading organisms and help combat infection. Eosinophils and basophils are white cells that respond to allergens or parasites.

- Most lymphocytes, another type of white cell, are found in the lymph nodes, the spleen and the lymphatic channels, but some enter the blood. There are three major types of lymphocytes: T lymphocytes (T cells), B lymphocytes (B cells) and natural killer (NK) cells. Each of these cells is a key part of the immune system.

Blood Cell & Lymphocyte Development

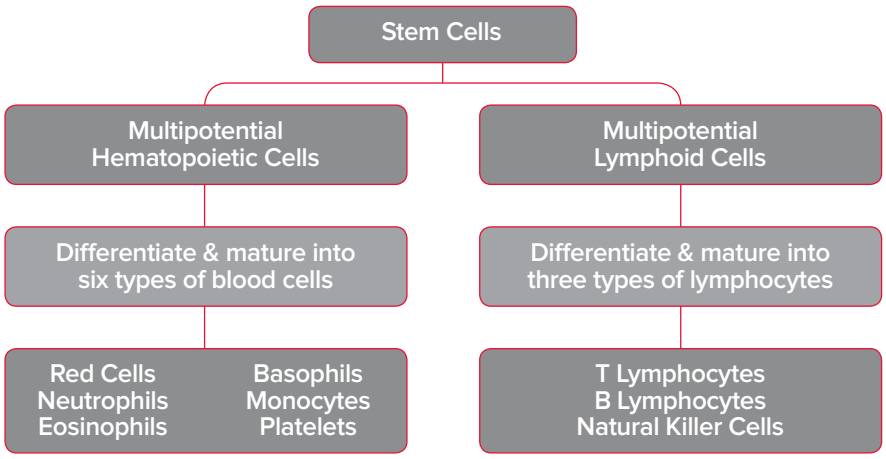


Figure 4. | Stem cells develop into blood cells (hematopoiesis) and lymphocytic cells.

Marrow is a spongy tissue where blood cell development takes place. It occupies the central cavity of bones. In newborns, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have functioning marrow. The spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull contain the marrow that makes blood cells in adults. The process of blood cell formation is called "hematopoiesis." A small group of cells, the stem cells, expand and then mature into all the blood cells in the marrow by the process of differentiation (see Figure 4 above).

In healthy individuals, there are enough stem cells to keep producing new blood cells continuously. Blood passes through the marrow and picks up the fully developed and functional red and white cells and platelets for circulation in the blood.

Some stem cells enter the blood and circulate. They are present in such small numbers that they cannot be counted or identified by standard blood count tests. Their presence in the blood is important because they can be collected by a special technique called "apheresis." There are also methods to induce more stem cells to leave their home in the marrow and circulate in the blood, allowing a greater

number of stem cells to be collected. If enough stem cells are harvested from a compatible donor, they can be transplanted into a recipient.

Stem cell circulation, from marrow to blood and back, also occurs in the fetus. After birth, placental and umbilical cord blood can be collected, stored and used as a source of stem cells for transplantation.

Medical Terms

Absolute Neutrophil Count. The number of neutrophils (a type of white cell) that a person has to fight infection. The absolute neutrophil count (ANC) is calculated by multiplying the total number of white blood cells by the percentage of neutrophils (segmented cells and bands).

Allogeneic Stem Cell Transplantation. A treatment that uses donor stem cells to restore a patient's marrow and blood cells. First, the patient is given conditioning therapy (high-dose chemotherapy or high-dose chemotherapy with total body radiation) to treat the blood cancer and to "turn off" the patient's immune system so that the donor stem cells will not be rejected. See also Reduced-Intensity Allogeneic Transplantation.

Anemia. A decrease in the number of red cells and, therefore, the hemoglobin concentration of the blood. This results in diminished ability of the blood to carry oxygen. If severe, anemia can cause a pale complexion, weakness, fatigue and shortness of breath on exertion.

Antibodies. Proteins released by plasma cells (derived from B lymphocytes) that recognize and bind to the specific foreign substances called "antigens." Antibodies coat, mark for destruction or inactivate foreign particles such as bacteria, viruses and harmful toxins. Antibodies can also be made in the laboratory in two ways. In the first method, material from one species is injected into a different species; the receiving species recognizes the material as foreign and makes antibodies to it. These antibodies are usually polyclonal antibodies; that is, they react to multiple targets (antigens).The second method involves monoclonal antibodies, which react to only one target (antigen) and can be used in several important ways. They can be used to identify and classify types of blood cancers, or they can be altered to make them useful in antibody-mediated immunotherapy.

Antigen. A foreign substance that enters the body and stimulates the production of complementary antibodies by plasma cells. A foreign substance may stimulate the response of T lymphocytes as well. When bacteria infect a tissue, the immune system recognizes them as foreign and causes the B lymphocytes to create antibodies against them. These antibodies attach to the antigen. This attachment of antibodies to their antigen facilitates the ingestion of bacteria by bacteria-eating

neutrophils (phagocytes). Transplanted cells can act to stimulate an immune response of a different type in which T lymphocytes of the recipient attack cells from the donor perceived as foreign, or T lymphocytes in the stem cell collection from the donor can attack the tissue cells in the recipient perceived as foreign. See Graft-Versus-Host Disease.

Apheresis. The process of removing certain components of a donor's blood and returning the unneeded parts to the donor. The process, also called "hemapheresis," circulates blood from a donor through a specialized machine and then back to the donor. Apheresis makes it possible to remove desired elements from large volumes of blood. Platelets, red cells, white cells and plasma can be removed separately. This procedure is also used to remove circulating blood stem cells, which can be frozen, stored and later used for transplantation instead of marrow stem cells.

Autologous Stem Cell Transplantation. A treatment that uses a patient's own stem cells to delay the progression of certain blood cancers. The autologous transplantation process takes place after the patient achieves a complete response (remission), or a good partial response, to induction drug therapy. In this treatment 1) the patient's stem cells are harvested, usually from the blood; 2) the stem cells are frozen for later use and the patient receives conditioning drug therapy; and 3) the stem cells are thawed and infused back into the patient through an indwelling catheter (central line). Patients receive supportive care to help prevent and/or manage the side effects. Generally, after 10 to 14 days, blood counts begin to normalize and the side effects of the conditioning therapy begin to resolve.

Basophil. A type of white cell that participates in certain allergic reactions.

B Lymphocyte. One of three specialized lymphocytes (white cells) that produce antibodies in response to any foreign substance, and especially to bacteria, viruses and fungi. These lymphocytes are a vital part of the immune system and are important in defense against infection. Some B lymphocytes mature into plasma cells, which are the principal antibody-producing cells.

Bone Marrow. A spongy tissue in the hollow central cavity of the bones that is the site of blood cell formation. After puberty, the marrow in the spine, ribs, breastbone, hips, shoulders and skull is most active in blood cell formation. In adults, the bones of the hands, feet, legs and arms do not contain blood-forming marrow. In these sites the marrow is filled with fat cells. When marrow cells have matured into blood cells, they enter the blood that passes through the marrow and are carried throughout the body.

Central Line. A special tube inserted into a large vein in the upper chest. The central line, sometimes referred to as an "indwelling catheter," is tunneled under the skin of the chest to keep it firmly in place. The external end of the catheter can be used to administer medications, fluids or blood products or to withdraw blood samples. With meticulous care, central lines can remain in place for long periods

of time (many months) if necessary. They can be capped and remain in place in patients after they leave the hospital, and be used for outpatient chemotherapy or blood product administration. Several types of catheters (for example, Groshong®, Hickman®, and Broviac®) can be used for patients receiving intensive chemotherapy or nutritional support. There are essentially two types of central lines: the one described above, in which the tube is outside the skin and requires daily care, and one called a "port," which is implanted completely under the skin. A port can be left in place indefinitely and can be removed when no longer needed. An alternative device, called a "PICC line," can be threaded to a large vessel from an arm vessel. See Peripherally Inserted Central Venous Catheter; Port.

Chemotherapy. The use of chemicals (drugs or medications) to kill malignant cells. Numerous chemicals have been developed for this purpose, and most act to injure the DNA of the malignant cells. When the DNA is injured, the cells cannot grow or survive. Successful chemotherapy depends on the fact that malignant cells are somewhat more sensitive to the chemicals than normal cells. These chemicals can cause injury to the gastrointestinal tract, skin and hair follicles causing the most common side effects of chemotherapy, such as mouth sores and hair loss.

Chromosome. Any of the 46 structures (in 23 pairs) in the nucleus of all cells in the human body (except the red blood cells and the egg and sperm cells) that contain a strand of DNA. This strand is made up principally of genes, which are specific stretches of the DNA. "Genome" is the term for an organism's complete set of DNA. The human genome has been estimated to contain about 30,000 genes. The genes on the X and Y chromosomes are the determinants of our gender: two X chromosomes produce a female and an X and a Y chromosome produce a male. Each chromosome has a long arm (called "q") and a short arm (called "p"). The number or size of chromosomes may be altered in blood cancer cells as a result of chromosome breakage and rearrangement (translocation). See Inversion; Translocation.

Clonal. The designation for a population of cells derived from a single transformed parent cell. Virtually all cancers are derived from a single cell with an injury (mutation) to its DNA and thus are monoclonal. Leukemia, lymphoma, myeloma and myelodysplastic syndromes are examples of clonal cancers; that is, cancers derived from a single abnormal cell.

Cluster Designation (CD). A term used with a number to identify a specific molecule on the surface of an immune cell. It is commonly used in its abbreviated form; for example, "CD20" (the target of the monoclonal antibody therapy rituximab [Rituxan®]) and "CD52" (the target of the monoclonal antibody therapy alemtuzumab [Campath®]).

Conditioning Treatment. Therapy before autologous or allogeneic transplantation with cytotoxic drugs, or drugs and total body radiation. The conditioning treatment serves several purposes. If a person is being treated for a blood cancer and receives high-dose conditioning treatment prior to an autologous or standard allogeneic

stem cell transplant, the conditioning treatment serves to greatly reduce any remaining tumor cells. It also markedly decreases the number of marrow cells. This may be important in order to open up the special niches that transplanted stem cells lodge in to engraft. Finally, if donor stem cells are used for standard allogeneic stem cell transplantation, the recipient's conditioning therapy severely depresses the lymphocytes that are the key cells in the immune system. This action helps to prevent the rejection of the stem cell graft by the recipient. Conditioning therapies for reduced-intensity allogeneic stem cell transplantation, which relies on donor immune cells to fight the patient's disease, do not completely destroy the patient's diseased marrow. Reduced-intensity conditioning regimens vary, and range from those of very low intensity to those only somewhat milder than high-dose conditioning regimens.

Cord Blood Stem Cells. Stem cells that are present in blood drained from the placenta and umbilical cord. These stem cells can repopulate the marrow of a compatible recipient and produce blood cells. Frozen cord blood is a source of donor stem cells for transplantation to HLA-matched recipients. Most cord blood transplants are done using matched or nearly matched unrelated donors.

Cryopreservation. A method used to keep frozen cells intact and functional for many years. Blood or marrow cells, including stem cells, can be stored for very long periods and remain functional if they are suspended in a liquid containing a chemical that prevents cellular injury during freezing or thawing. This chemical is referred to as a "cryoprotective" agent. Dimethyl sulfoxide (DMSO) is one of the most commonly used agents. The freezing temperature is much lower (colder) than that of a household freezer.

Cycle of Treatment. An intensive, clustered period of chemotherapy and/or radiation therapy. The treatment may be given for several days or weeks. The treatment plan may call for two, three or more cycles of treatment.

Differentiation. See Hematopoiesis.

DNA. The abbreviation for "deoxyribonucleic acid," the material inside the nucleus of cells that carries genetic information. Genes tell the cell how to make the proteins that enable the cell to carry out its functions. DNA can become highly abnormal in cancer cells.

Donor Lymphocyte Infusion (DLI). A therapy that involves giving lymphocytes from the original stem cell donor to a patient who has had a remission after an allogeneic stem cell transplant, followed by a relapse of disease. DLI may induce an immune reaction against the patient's cancer cells.

Engraftment. The process in which transplanted donor stem cells migrate to the recipient's marrow and then produce blood cells of all types. This result is first evident when new white cells, red cells and platelets begin to appear in the recipient's blood following transplantation.

Eosinophil. A type of white cell that participates in allergic reactions and helps to fight certain parasitic infections.

Erythrocyte. See Red Cell.

Extracorporeal Photopheresis. A procedure being studied to treat steroid-refractory graft-versus-host disease (GVHD). The procedure involves a series of treatments. Blood is removed through a vein and then treated with methoxsalen (Uvadex®), a drug that sensitizes the cells to ultraviolet (UV) light. UVA rays are used to irradiate the cells, which are then reinfused into the patient.

Fractionation of the Dose. A strategy intended to minimize the significant side effects of total body irradiation conditioning therapy. The required dose of radiation is given in several smaller doses daily rather than in one larger dose. This approach has decreased the adverse effects of the treatment.

Genome. See Chromosome.

Graft-Versus-Host Disease (GVHD). The immune attack by lymphocytes in a donor's marrow or blood cell suspension (the graft) against the tissues of the recipient (the host). The immune cells most engaged in this reaction are the T lymphocytes present in the donor's blood or marrow, the source of the stem cells. The principal sites of injury to the patient are the skin, the liver and the gastrointestinal tract. The reaction does not occur in identical twin transplants. The reaction may be minimal in closely matched individuals or severe in less well-matched individuals. These reactions are mediated in part by antigens that are not in the major HLA system and cannot be matched prior to transplantation. For example, in the case of a female stem cell donor and a male recipient, factors produced by genes on the male recipient's Y chromosome may be seen as foreign by the female donor's cells, which do not share the genes on the Y chromosome. This fact does not prohibit female donors and male recipients, but it makes the risk of immune reaction higher. See HLA.

Graft-Versus-Tumor (GVT) Effect. The potential immune reaction by which transplanted (donor) T lymphocytes recognize and attack the malignant cells of the recipient (host). This effect was noted when 1) disease recurrence after transplant was seen to be more likely if the donor and recipient were identical twins than if they were nonidentical siblings; 2) disease recurrence was less likely the more pronounced the graft-versus-host disease (GVHD) was; and 3) the removal of donor T lymphocytes decreased the incidence of GVHD but also resulted in a higher frequency of disease relapse. Each of these observations could be explained best by an immune attack by donor T lymphocytes against recipient tumor cells that, along with the intensive conditioning treatment, serves to keep the disease in check. This effect seems to be most active in types of myeloid leukemia, although it may also occur in patients with other blood cancers. See HLA.

Granulocyte. A type of white cell that has a large number of prominent granules in the cell body. Neutrophils, eosinophils and basophils are types of granulocytes.

Granulocyte-Colony Stimulating Factor (G-CSF). See Growth Factor.

Growth Factor. A chemical used to stimulate the production of neutrophils and shorten the period of low neutrophil counts in the blood after chemotherapy. Granulocyte-colony stimulating factor (G-CSF) and granulocyte-macrophage colony-stimulating factor (GM-CSF) are examples of growth factors that are made commercially. GM-CSF can also stimulate monocytes.

Haplotype. The tissue type passed on by parent to offspring, representing the genes on one parental chromosome. A transplant procedure between a sibling donor and a recipient who are haploidentical (both carry that same one parental chromosome) is sometimes possible if the underlying disease makes it worth risking partial compatibility. Conditioning of the recipient and lymphocyte depletion of the donor stem cell collection are steps taken to reduce the risk of immune cell activation caused by the tissue-type differences.

Hemapheresis. See Apheresis.

Hematologist. A doctor who specializes in the treatment of blood cell diseases. This person is either an internist, who treats adults, or a pediatrician, who treats children.

Hematopathologist. See Pathologist.

Hematopoiesis. The process of blood cell development in the bone marrow. The most undeveloped cells in the marrow are stem cells. They start the process of blood cell development. The stem cells begin to develop into young or immature blood cells such as red cells or white cells of various types. This process is called "differentiation." The young or immature blood cells then further develop into fully functional blood cells. This process is called "maturation."

The mature cells leave the marrow, enter the blood and circulate throughout the body. Hematopoiesis is a continuous process that is active normally throughout life. The reason for this activity is that most blood cells live for short periods and must be steadily replaced. Red cells die in four months, platelets in 10 days and most neutrophils in one to three days. About 500 billion blood cells are made each day. When the marrow is invaded with cancer cells, the constant demand for new blood cells cannot be met, resulting in a severe deficiency in blood cell counts.

HLA. The abbreviation for "human leukocyte-associated antigen(s)." These antigens are proteins on the surface of most tissue cells, and they give an individual his or her unique tissue type. HLA factors are inherited from mother and father, and the greatest chance of having the same HLA type is between siblings. On average, one in four siblings is expected to share the same HLA type. The testing for HLA

factors is referred to as "tissue typing." There are six major groups of HLA: A, B, C, D, Dr, and Dq. These proteins on the cell surface act as antigens when donated (transplanted) to another individual, the recipient. If the antigens on the donor cells are identical (as in identical twins) or very similar (as in HLA-matched siblings), the transplant (donated stem cells) is more likely to survive (engraft) in the recipient. In addition, the recipient's body cells are less likely to be attacked by the donated immune cells. See Graft-Versus-Host Disease.

Host. The person into whom donated living cells are or will be transplanted.

Immune System. Cells and proteins that defend the body against infection. Lymph nodes, lymphocytes and the spleen are some parts of the body's immune system.

Immunosuppression. A state in which the immune system does not function properly and its protective functions are inadequate. The patient is more susceptible to infections, including those from microbes that are usually not highly infectious (see Opportunistic Infection). This can occur as a result of intensive chemotherapy and radiation therapy, especially when used in high doses to condition a patient for transplantation. It also can occur because of disease states. Human immunodeficiency virus (HIV) infection is one such disease. Graft-versus-host disease (GVHD) creates immunosuppression. In the transplant patient the conditioning regimen and severe GVHD can result in overwhelming infection. See Graft-Versus-Host Disease.

Indwelling Catheter. See Central Line.

Interstitial Pneumonitis. A severe inflammation in the lungs that can occur as a toxic effect of total body radiation in the conditioning regimen. The small airways and intervening spaces between air sacs get congested and swollen, and exchange of oxygen can be compromised. Typically, no infection is present, although a similar reaction can occur as a result of infection.

Intrathecal. Designation for the space between the covering or lining of the central nervous system and the brain or spinal cord. The lining is called the "meninges." In some situations drugs have to be administered directly into the spinal canal when cancer cells are present in the meninges. This is called "intrathecal therapy."

Inversion. An abnormality of chromosomes that occurs when a section of a chromosome breaks and turns upside down, so that its genetic material is in reverse order but the inverted piece remains attached to the chromosome. See Chromosome.

Leukocyte. See White Cell.

Leukopenia. A decrease below normal in the number of blood leukocytes (white cells).

Lymph Nodes. Small structures, usually less than 1 centimeter, that contain large numbers of lymphocytes and are connected with each other by small channels called "lymphatics." These nodes are distributed throughout the body. In patients with non-Hodgkin lymphoma, Hodgkin lymphoma and some types of lymphocytic leukemia, the malignant lymphocytes grow and the lymph nodes become enlarged. This enlargement of lymph nodes can be seen, felt or measured by computed tomography (CT) scan or magnetic resonance imaging (MRI), depending on the location and degree of enlargement.

Lymphocyte. A type of white cell that is the essential cell type in the body's immune system. There are three major types of lymphocytes: B lymphocytes, which produce antibodies to help combat infectious agents like bacteria, viruses and fungi; T lymphocytes, which have several functions, including assisting B lymphocytes to make antibodies; and natural killer (NK) cells, which can attack virus-infected cells or tumor cells.

Marrow. See Bone Marrow.

Maturation. See Hematopoiesis.

Meninges. See Intrathecal.

Monoclonal Antibodies. Antibodies made by cells belonging to a single clone. These highly specific antibodies can be produced in the laboratory. They are very important reagents for identifying and classifying disease by immunophenotyping cells. They also have clinical applications for targeted delivery of drugs to leukemia or lymphoma cells and can be used to purify cells obtained for stem cell transplants.

Monocyte/Macrophage. A type of white cell that represents about 5 to 10 percent of the cells in normal human blood. The monocyte and the neutrophil are the two major microbe-eating and microbe-killing cells in the blood. When monocytes leave the blood and enter the tissue, they are converted to macrophages. The macrophage is the monocyte-in-action: It can combat infection in the tissues, ingest dead cells (in this function it is called a "scavenger cell") and assist lymphocytes in their immune functions.

Mucous Membranes. The inner lining of cavities such as the mouth, nose and sinuses. These linings require new cells to be made to replace those that drop off. This replacement is a normal process and keeps the lining intact and moist. Radiation therapy or chemotherapy drugs that block cells from dividing prevent the replacement of lost cells. The linings become dry and defective and may ulcerate in patients who receive such treatment. This change can be painful, as when ulcers develop in the mouth. These painful, ulcerating lesions are referred to as oral "mucositis." Anal ulcers can also develop. The loss of what is referred to as the "barrier" function of mucous membranes permits microbes to enter the tissue or blood and often leads to infection.

Mutation. An alteration in a gene that results from a change to some part of the DNA that represents the gene. A "germ cell mutation" is present in the egg or the sperm and can be transmitted from parent to offspring. A "somatic mutation" occurs in a specific tissue cell and can result in the growth of that cell into a tumor. Most cancers start after a somatic mutation. In leukemia, lymphoma and myeloma, a primitive marrow (blood-forming) or lymph node cell undergoes one or more somatic mutations that lead to the formation of a tumor. If a mutation results from a major abnormality of chromosomes, such as a translocation, it can be detected by cytogenetic examination. Sometimes the alteration in the gene is more subtle and requires more sensitive tests to identify the original mutated cell. See Oncogene.

Myeloablation. The severe or complete depletion of bone marrow cells, as in the administration of high doses of chemotherapy or radiation therapy prior to standard allogeneic stem cell transplantation. Myeloablative therapy completely eliminates an individual's ability to make blood cells.

Neutropenia. A decrease below normal in the number of blood neutrophils, a type of white cell.

Neutrophil. The principal phagocyte (microbe-eating cell) in the blood. This blood cell is the main cell that combats infection. Often, it is not present in sufficient quantities in patients with acute leukemia or after chemotherapy, thus increasing susceptibility to infection. A neutrophil may be called a "poly" (for polymorphonuclear) or "seg" (for segmented nucleus).

Nonmyeloablative Stem Cell Transplantation. See Reduced-Intensity Allogeneic Transplantation.

Oncogene. A mutated gene that is the cause of a cancer. Several subtypes of acute myeloid leukemia, acute lymphoblastic leukemia and lymphoma, and nearly all cases of chronic myeloid leukemia, are associated with an oncogene. See Mutation.

Oncologist. A doctor who diagnoses and treats patients with cancer. Oncologists are usually internists who treat adults or pediatricians who treat children. Radiation oncologists specialize in the use of radiation to treat cancer, and surgical oncologists specialize in the use of surgical procedures to diagnose and treat cancer. These doctors cooperate and collaborate to provide the best treatment plan (surgery, radiation therapy, chemotherapy or immunotherapy) for the patient.

Opportunistic Infection. Any unusual infections to which patients treated for cancer may be susceptible because of the suppression of their immune system. The word "opportunistic" is used to describe infections with bacteria, viruses, fungi or protozoa to which individuals with a normal immune system are not susceptible. The infecting organisms take advantage of the opportunity provided by immunodeficiency, especially when coupled with very low white cell counts resulting from therapy or the disease itself.

Pancytopenia. A decrease below normal levels in the concentration of the three major blood cell structures: red cells, white cells and platelets.

Pathologist. A doctor who identifies disease by studying tissues under a microscope. A hematopathologist is a type of pathologist who studies diseases of blood cells by looking at peripheral blood smears, bone marrow aspirates and biopsies, and lymph nodes and other tissues and uses his or her expertise to identify diseases. In addition to the microscope, a hematopathologist uses laboratory values, flow cytometry and molecular diagnostic tests to make the most accurate diagnosis. The hematopathologist works closely with the hematologist or oncologist who sees the patient and decides on the best treatment based upon the diagnosis. See Hematologist.

Peripherally Inserted Central Venous Catheter (PICC or PIC Line). A long, thin, flexible tube that is inserted into the body and can be left in place for weeks or even months for administration of medications, fluids and nutrition. It can also be used to obtain blood samples. Prior to insertion of the PICC, the patient is given a local anesthetic to numb the arm between the elbow and the shoulder. The PICC is inserted through the skin into a vein in the arm and advanced until it reaches the superior vena cava just above the heart. The superior vena cava is one of the veins in the central venous system. The PICC eliminates the need for standard intravenous (IV) administration.

Phagocyte. A cell that readily eats (ingests) microorganisms such as bacteria and fungi and kills them as a means of protecting the body against infection. The two principal phagocytes are neutrophils and monocytes. They leave the blood and enter tissues in which an infection has developed. A severe decrease in the concentrations of these cells is the principal cause of susceptibility to infection in patients treated with intensive radiation therapy and/or chemotherapy. Treatment may suppress blood cell production in the marrow, resulting in deficiencies of these phagocytic cells.

PICC or PIC line. See Peripherally Inserted Central Venous Catheter.

Platelet. Small blood cells (about one-tenth the volume of red cells) that stick to the site of blood vessel injury, aggregate and then seal off the injured blood vessel to stop bleeding. "Thrombocyte" is a synonym for platelet, and a form of this word is often used as the prefix in describing disorders of platelets, such as thrombocytopenia (too few) or thrombocythemia (too many).

Platelet Transfusion. The transfusion of donor platelets, which may be needed to support some patients treated for blood cancer. The platelets can be collected from several unrelated donors and given as pooled, random-donor platelets. The platelets from about five single-unit blood donors are required to significantly raise the platelet count in a recipient. Sufficient platelets can be obtained from one donor by a procedure known as "apheresis." The platelets are skimmed from large volumes of blood passing through a specialized machine. The red cells and plasma

are returned to the donor. The advantage of single-donor platelets is that the patient is not exposed to the spectrum of antigens on platelets from many different people and thus is less likely to develop antibodies against donor platelets. HLA-matched platelet transfusion can be given from a related donor who has an identical or very similar HLA tissue type.

Port. A small device used with a central line to allow access to a vein. The port is placed under the skin of the chest. After the site heals, no dressings are needed. To give medicines or nutrition or to take blood samples, the doctor or nurse inserts a needle through the skin into the port. A numbing cream can be put on the skin before the port is used. Ports must be flushed periodically. Patients and/or caregivers are given instructions about caring for the port. See Central Line.

Red Cell. A blood cell that carries the red-colored protein hemoglobin, which binds oxygen and delivers it to the tissues of the body. The red cells make up about 40 to 45 percent of the volume of the blood in healthy individuals. Another term for red cell is "erythrocyte."

Reduced-Intensity Allogeneic Stem Cell Transplantation. A form of allogeneic transplantation, now in clinical trials. In reduced-intensity transplantation (also called "nonmyeloablative stem cell transplantation"), patients receive lower doses of chemotherapy drugs and/or radiation in preparation for the transplant. Immunosuppressive drugs are used to prevent rejection of the graft (donor tissue). The engraftment of donor immune cells may allow these cells to attack the disease (graft-versus-disease effect).

Refractory Disease. Disease that does not go into remission or improve substantially after initial standard therapy. See Resistance to Treatment.

Relapse/Recurrence. The return or progression of disease that initially responded to therapy.

Remission. A disappearance of evidence of a disease, usually as a result of treatment. The words "complete" and "partial" are sometimes used to further describe remission. Complete remission means that all evidence of the disease is gone. Partial remission means that the disease is markedly improved by treatment, but that some evidence of the disease remains. Long-term benefit usually requires a complete remission, especially in acute leukemia or progressive lymphoma.

Resistance to Treatment. The ability of cells to grow despite exposure to a chemical that ordinarily kills cells or inhibits their growth. Refractory disease is the condition in which a proportion of malignant cells resist the damaging effects of a drug or drugs. Cells develop drug resistance in several different ways.

Scavenger Cell. See Monocyte.

Spleen. An organ located in the left upper portion of the abdomen just under the left side of the diaphragm. It contains clusters of lymphocytes and also filters old or worn-out cells from the blood. It is often affected in lymphocytic leukemia and lymphoma. Enlargement of the spleen is called "splenomegaly." Surgical removal of the spleen is known as "splenectomy." Certain diseases are treated by removing the spleen. Most of the functions of the spleen can be performed by other organs, such as the lymph nodes and liver, but a person whose spleen has been removed is at higher risk for infection. He or she is given antibiotic therapy immediately at the first sign of infection, such as a fever.

Stem Cells. Primitive cells in marrow that are essential to the formation of red cells, white cells and platelets. Stem cells are largely found in the marrow, but some leave the marrow and circulate in the blood. Using special techniques, the stem cells in the blood can be collected, preserved by freezing and later thawed and used for stem cell therapy. See Hematopoiesis.

Thrombocyte. See Platelet.

Thrombocythemia. An increase above normal in the number of blood platelets (thrombocytes).

Thrombocytopenia. A decrease below normal in the number of blood platelets (thrombocytes).

T-Lymphocyte Depletion. A process to decrease the number of immune cells that cause GVHD (graft-versus-host disease). Typically, antibodies against T lymphocytes are used to draw these cells out of the stem cell sample to be used for transplant. The decreased presence of T lymphocytes in the transplant minimizes the intensity of GVHD. T lymphocytes are depleted only in certain circumstances, because T lymphocytes are also beneficial. They help the donated stem cells take hold (engraft) and grow in the recipient's marrow. In some cases, T lymphocytes attack blood cancer cells, enhancing the results of other treatment. This "graft-versus-tumor effect" can be seen mostly in the myeloid leukemias. The attack on the remaining blood cancer cells makes it less likely that the disease will return after transplant.

Translocation. An abnormality of chromosomes in marrow or lymph node cells that occurs when a piece of one chromosome breaks off and attaches to the end of another chromosome. In a balanced translocation, genetic material is exchanged between two different chromosomes with no gain or loss of genetic information. When a translocation takes place, the gene at which the break occurs is altered. This is one form of somatic mutation that may transform the gene into an oncogene (cancer-causing gene). See Mutation.

Veno-occlusive Disease (VOD). A disease that may be a complication following high-dose chemotherapy and/or radiation, in which the blood vessels that carry blood through the liver swell and become clogged.

White Cell. Any of the five major types of colorless, infection-fighting cells in the blood: neutrophils, eosinophils, basophils, monocytes and lymphocytes. Another term for white cell is "leukocytes."

More Information

Free LLS publications include

Choosing a Blood Cancer Specialist or Treatment Center
Understanding Clinical Trials for Blood Cancers
Understanding Lab and Imaging Tests
Understanding Side Effects of Drug Therapy

Visit "Suggested Reading" at www.LLS.org/resourcecenter to see helpful books on a wide range of topics.

Resources

The American Society for Blood and Marrow Transplantation (ASBMT)
(847) 427-0224
www.asbmt.org

ASBMT is an international professional association that promotes the advancement of blood and marrow transplantation both in clinical practice and in research.

The Center for International Blood and Marrow Transplant Research (CIBMTR)
(414) 805-0700
www.cibmtr.org

CIBMTR leads a worldwide collaboration of scientists and clinicians to advance understanding and outcomes of hematopoietic cell transplantation. This research helps assess donor safety and helps identify the most promising transplant approaches and the patients most likely to benefit from this therapy.

Be The Match, operated by the National Marrow Donor Program® (NMDP)
(888) 999-6743
www.BeTheMatch.org

Be The Match helps patients with leukemia, lymphoma and other diseases who need a marrow or umbilical cord blood transplant. People can join the Be The Match registry - the largest listing of potential marrow donors and donated cord blood units - contribute financially, and volunteer. Patients and their families can also turn to Be The Match for support and resources before, during and after transplant.

Posttransplant care guidelines have been developed for patients and can be accessed at www.bethematch.org/patient.

National Bone Marrow Transplant Link (nbmtLINK)
(800) 546-5268
www.nbmtlink.org

The mission of the National Bone Marrow Transplant Link is to help patients, caregivers, and families cope with the social and emotional challenges of bone marrow/stem cell transplant from diagnosis through survivorship by providing vital information and personalized support services.

References

Appelbaum FR, Forman SJ, Negrin RS, Blume KG, eds. *Thomas' Hematopoietic Cell Transplantation.* 4th ed. Oxford, England: Blackwell Publishing Ltd; 2007.

Jagasia MH, Arora M, Flowers ME, et al. Risk factors for acute GvHD and survival after hematopoietic cell transplantation. *Blood.* 2011;119(1):296-307.

Lowsky R, Negrin RS. Principles of hematopoietic cell transplantation." In: Lichtman MA, Kipps TJ, Seligsohn U, Kaushansky K, Prchal JT, eds. *Williams Hematology.* 8th ed. Available at AccessMedicine. Accessed December 15, 2012.

Majhail NS, Rizzo JD, Lee SJ, et al. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. *Bone Marrow Transplantation.* 2012;47(3):337-341.

National Marrow Donor Program. HLA matching: finding the best donor or cord blood unit. Available at: http://marrow.org/Patient/Transplant_Process/Search_Process/HLA_Matching__Finding_the_Best_Donor_or_Cord_Blood_Unit.aspx. Accessed December 12, 2012.

National Marrow Donor Program, Key Messages, Facts & Figures. Updated January 2012. Available at: http://marrow.org/News/Media/Facts_and_Figures_%28PDF%29.aspx. Accessed December 15, 2012.

Spellman SR, Eapen M, Logan BR, et al. A perspective on the selection of unrelated donors and cord blood units for transplantation. *Blood.* 2012;120(2):259-265.

LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

REACH OUT TO OUR **INFORMATION SPECIALISTS**

The Leukemia & Lymphoma Society's (LLS) Information Specialists provide patients, families and healthcare professionals with the latest information on leukemia, lymphoma and myeloma.
Our team consists of master's level oncology social workers, nurses and health educators who are available by phone Monday through Friday, 9 am to 9 pm (ET).

Co-Pay Assistance
LLS's Co-Pay Assistance Program helps blood cancer patients cover the costs of private and public health insurance premiums, including Medicare and Medicaid, and co-pay obligations. Support for this program is based on the availability of funds by disease.
For more information, call 877.557.2672 or visit www.LLS.org/copay.

For a complete directory of our patient services programs, contact us at
800.955.4572 or **www.LLS.org**
(Callers may request a language interpreter.)

LEUKEMIA & LYMPHOMA SOCIETY®

fighting blood cancers

For more information, please
contact our Information Specialists
800.955.4572 (Language interpreters
available upon request)
www.LLS.org

or:

National Office
3 International Drive, Suite 200
Rye Brook, NY 10573

Our Mission:

Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families.

LLS is a nonprofit organization that relies on the generosity of individual, foundation and corporate contributions to advance its mission.

PS40 30M 6/16