LEUKEMIA & LYMPHOMA SOCIETY®

PROVIDING THE LATEST INFORMATION FOR PATIENTS & CAREGIVERS

Blood and Marrow Stem Cell Transplantation

Revised **2023**

A six-word narrative about living with blood cancer from patients in our LLS Community

Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/ happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith, and optimism. Finding joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.

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www.LLS.org/Community

Join our online social network for people who are living with or supporting someone who has a blood cancer. Members will find:

- **Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff**
- **Accurate and cutting-edge disease updates**
- **The opportunity to participate in surveys that will help improve care**

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Acknowledgement

The Leukemia & Lymphoma Society appreciates the review of this material by:

Trent Peng Wang, DO
Assistant Professor, University of Miami Miller School of Medicine
Cellular Therapy, Hematology Oncology
University of Miami Health System
Miami, FL

Introduction

Hematopoietic stem cell transplantation (also known simply as "stem cell transplantation") is a treatment in which a patient receives healthy stem cells to replace stem cells that have been destroyed by disease or by high doses of chemotherapy and/or radiation therapy. This booklet provides information about stem cell transplantation for the treatment of blood cancers (leukemia, lymphoma, myeloma, myelodysplastic syndromes and myeloproliferative neoplasms). Brief descriptions of normal blood and bone marrow, and definitions of medical terms are also included.

About 20,000 stem cell transplantation procedures are performed in the United States every year. Worldwide, approximately 60,000 transplant procedures are performed annually. As transplantation procedures and supportive care practices have advanced, stem cell transplantation has become safer, and patient survival continues to improve. Stem cell transplantation may help patients live longer and may also offer the possibility of a cure for certain blood cancers that are otherwise considered incurable.

New treatments may have been approved since this book was printed. Check www.LLS.org/DrugUpdates or call (800) 955-4572.

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Overview

For thousands of people with blood cancers, stem cell transplantation (SCT) is a potentially life-saving treatment option. Most patients who undergo SCT have blood cancers such as leukemia, lymphoma, myeloma, myelodysplastic syndromes and myeloproliferative neoplasms. Patients with non-malignant hematologic disorders (such as sickle cell disease or bone marrow failure syndromes) may also benefit from SCT.

Hematopoietic stem cell transplantation (HSCT) is a procedure that infuses healthy blood stem cells into the body to replace damaged or diseased stem cells. Normal blood stem cells, also called "hematopoietic stem cells," are immature cells that produce all the blood cells in the body. Normal blood stem cells can either divide to form more blood-forming stem cells or they can mature into:

- Red blood cells that carry oxygen throughout the body

- White blood cells that help fight infections and diseases such as cancer
- Platelets that help control bleeding

All blood cells in the body begin as immature stem cells in the bone marrow, the spongy tissue found in the central cavity of certain bones. Red blood cells, platelets and most white blood cells are formed in the bone marrow. Blood stem cells are constantly dividing and changing into different types of blood cells, replacing older worn-out blood cells. Stem cells generate billions of new blood cells every day.

The production of all the body's blood cells depends on the stem cells, the source of all the blood cells in the body. When cancer or cancer treatment destroys a patient's stem cells, the patient is no longer able to produce the blood cells that are necessary for life. If the bone marrow cannot make enough new blood cells, many health problems may occur. These problems include infections, bleeding, or anemia, and can be serious enough to cause death. Stem cell transplantation can replace damaged and diseased stem cells with healthy stem cells and restore the bone marrow's ability to make new blood cells.

Blood stem cells are normally found in the:

- Bone marrow, where most stem cells are located
- Peripheral blood, the blood circulating throughout the body
- Umbilical cords of newborn babies

Stem cells from any of these sources can be used in stem cell transplantation. If the stem cells are collected from bone marrow, the procedure is called "bone marrow transplantation"; when the stem cells are collected from peripheral blood, it is called a "peripheral blood stem cell transplantation"; and if stem cells are collected from an umbilical cord, it is known as an "umbilical cord blood transplantation." Peripheral blood is the most common source of stem cells for transplantation.

To prepare for a stem cell transplantation, patients receive what is called a "conditioning regimen" that consists of chemotherapy and sometimes radiation therapy. The conditioning regimen is designed to:

- Destroy cancer cells in patients with blood cancers and to destroy damaged stem cells in patients with diseases such as aplastic anemia
- Destroy blood-forming cells in the bone marrow to create space for the new, healthy stem cells
- Suppress the patient's immune system to prevent rejection of new stem cells (if the patient receives stem cells from a donor)

The conditioning regimen, however, also may destroy the stem cells that the body needs to make new blood cells. To replace these stem cells, patients receive infusions of healthy stem cells. There are two main types of transplantation:

- Autologous transplantation, in which patients own stem cells are removed and returned to their own body after a conditioning regimen
- Allogeneic transplantation, in which patients receive stem cells from someone other than themselves, such as a relative or an unrelated donor

After the stem cells are infused (transplanted) into the patient's bloodstream, they travel to the bone marrow and begin the process of forming new, healthy blood cells including white blood cells, red blood cells and platelets. This process is called "engraftment."

While a stem cell transplant can be a cure for numerous patients, it is very hard on a patient's body. It can lead to severe complications or even death. It is important for patients to discuss all potential treatment options and the associated risks and side effects with the members of their healthcare team to determine if stem cell transplantation is a treatment option for them.

The number of people who receive stem cell transplants continues to increase due to improvements in transplantation technology and supportive care, the introduction of newer indications that allow older patients to be eligible for transplantation, and greater use of alternative donors. The estimated number of stem cell transplants in North America in 2020, by blood cancer type, is shown in **Table 1**, on page 5.

Transplant Eligibility

Stem cell transplantation has been used to cure thousands of people who have cancer, but there are serious risks to this treatment. Medical complications can be life-threatening, and the transplant process can also be difficult emotionally. It often requires a lengthy hospital stay and isolation from friends and family. Before undergoing stem cell transplantation, patients considering this treatment should discuss the risks and benefits with their doctors. Patients should also ask members of their healthcare team about other treatment options.

Not all patients are eligible for stem cell transplantation because not all patients can withstand the conditioning regimen and/or the side effects of treatment.

- High-dose conditioning regimens have been known to place great stress on the body and to cause serious damage to organs such as the heart, liver, gastrointestinal tract, kidneys, brain and lungs. See *Conditioning* on page 30.

Estimated Number of Stem Cell Transplants in North America, by Blood Cancer Type, in 2020

	Allogeneic (related/unrelated donor)				**Autologous** (patient's own cells)			
	Cell Source				**Cell Source**			
Disease Category	**Bone Marrow**	**Cord Blood**	**Peripheral Blood**	**Grand Total**	**Bone Marrow**	**Cord Blood**	**Peripheral Blood**	**Grand Total**
Acute Lymphoblastic Leukemia (ALL)	283	92	1,036	1,411	1	0	2	3
Acute Myeloid Leukemia (AML)	366	160	2,847	3,373	0	0	27	27
Chronic Myeloid Leukemia (CML)	36	7	225	268	0	0	0	0
Hodgkin Lymphoma (HL)	25	0	104	129	0	0	803	803
Leukemia, other	7	6	99	112	0	0	1	1
Multiple Myeloma/ Plasma Cell disease	2	1	96	99	13	0	8,110	8,123
Myelodysplastic Syndromes (MDS)	109	28	1,111	1,248	0	0	2	2
Myelodysplastic/ Myeloproliferative Neoplasms (MDS/MPN)	22	8	187	217	0	0	0	0
Myeloproliferative Neoplasms (MPNs)	10	8	430	448	0	0	0	0
Non-Hodgkin Lymphoma	68	16	535	619	1	0	2,564	2,565
	Allogeneic Total			7,924	**Autologous Total**			11,524
	Combined Total							19,448

Table 1. This table provides the estimated number of stem cell transplants used to treat blood cancers in North America. Included are the totals for each type of transplant by disease category, as well as the grand totals for both types of transplants.

Source: *Adapted from Center for International Blood and Marrow Transplant Research (CIBMTR). Table 16: Number of HCTs (hematopoietic cell transplantations) performed in the United States and reported to CIBMTR, cell source and disease category by donor type and year, 2016-2020.* https://bloodstemcell.hrsa.gov/data/donation-and-transplantation-statistics/transplant-activity-report#summary

- High-dose conditioning regimens destroy the stem cells that create white blood cells that are a part of the body's immune system. This compromises the body's immune system, leaving patients extremely vulnerable to serious infection.
- Patients receiving an allogeneic transplant (stem cells from a donor) are at risk for graft-versus-host disease (GVHD), a potentially serious complication that can affect quality of life and even cause death (see *Graft-Versus-Host Disease* on page 35).
- Medications used for immune suppression can also be toxic to patients.

Some patients who have other major health problems may also not be eligible for standard transplantation. For some of these patients, however, a reduced-intensity allogeneic stem cell transplant may be a treatment option (see *Reduced-Intensity Allogeneic Stem Cell Transplantation* on page 19).

In order to determine if a patient is a good candidate for a stem cell transplantation, the patient's healthcare team will consider:

- The patient's general health and medical condition
- The patient's type and stage of cancer or disease
- The patient's prior treatment history
- The likelihood that the disease will respond to the transplant
- The availability of a suitable donor (for allogeneic transplant) or the ability to use the patient's own stem cells (for autologous transplant)

Other factors, such as the availability of a caregiver after the patient's release from the hospital, are also taken into consideration to determine whether a patient is a good candidate for transplantation.

The risks of stem cell transplantation have decreased over the passing few decades. Ongoing research continues to improve the procedure. For numerous diseases and patients, however, effective new drugs and new types of therapies may be better treatment options than stem cell transplantation. Doctors and their patients will consider many factors when deciding whether stem cell transplantation is the best treatment option.

Age and Transplantation. Younger patients often have more successful transplants. About three-quarters of people who develop blood cancer, however, are older than age 50. In general, older individuals are more likely to have:

- Complicating medical problems
- Difficulty treating GVHD after transplantation
- Decreased tolerance for the cumulative effects of intensive chemotherapy and radiation treatments needed before the transplant

New developments in transplantation with less toxic conditioning regimens such as reduced-intensity stem cell transplantation (see *Reduced-Intensity Allogeneic Stem Cell Transplantation* on page 19), better supportive care, and infection control measures have allowed many older patients to be candidates for stem cell transplantation. There is no specific upper-age limit for most standard stem cell transplantations (although some transplant centers may have age limits). The number of autologous and allogeneic transplants for the treatment of malignant diseases in older patients has increased steadily over the past two decades. In 2020, 37% of autologous transplant recipients for lymphomas and multiple myeloma were 65 or older and 27% of allogeneic transplant recipients were 65 or older.

Timing of Transplantation and Tissue Typing. Stem cell transplantation, once regarded as a therapy of last resort, is now considered a life-saving treatment for thousands of patients. It is being used earlier in the course of treatment for diseases that typically cannot be controlled by non-stem cell therapies. The points at which transplant options are considered during an individual's disease course varies.

In numerous cases, the success of a transplant depends on appropriate timing. For select patients, transplantation is recommended during their first remission. For others, transplantation may be recommended later during the course of treatment, for example if there is disease that has relapsed (recurred, returned) or is refractory (resistant), or if there has been poor response to treatment. This decision may depend on the response to initial therapy of the underlying disease.

If allogeneic transplantation is a consideration, it is best to have the patient's tissue typing (human leukocyte antigen [HLA] typing) done early in the disease course. See *Tissue Typing for Allogeneic Stem Cell Transplantation* on page 21.

The patient's siblings should also have tissue typing done. If the patient does not have a sibling HLA match, then a decision can be made about whether to enter the patient's HLA type into an unrelated donor registry. Entering into an unrelated donor registry will determine whether a suitable unrelated donor match might be available. If needed, cord blood match, mismatch, or half-matched (parent/child) donor transplants may also an option.

Overview: Stem Cell Transplantation Options for Patients Who Have Blood Cancers

The following information is a general summary and is not all-inclusive. Each patient has unique circumstances, so patients should discuss all appropriate therapies with their doctors. For more detailed information, see the free LLS booklets for each of the blood cancers listed here. *Note: in all the following cases, wherever the term "suitable donor" is used, a suitable donor may also be a matching cord blood stem cell donor.*

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.
- An allogeneic stem cell transplant may be an option for patients with standard-risk or high-risk ALL whose disease is in remission for the first time or whose disease is in partial remission (provided a suitable donor is available).
- Autologous stem cell transplantation outside of the clinical-trial setting is not recommended as treatment for ALL.
- Most children with ALL (about 75 to 80 percent) do not need stem cell transplantation. A child with refractory disease or relapsed ALL may be considered for allogeneic transplantation.

Acute myeloid leukemia (AML)

- Favorable-risk AML: Stem cell transplantation is generally not recommended with first complete remission.
- Intermediate-risk AML: Patients with intermediate-risk AML should discuss standard and/or reduced-intensity stem cell allogeneic transplantation with their doctor to determine if one of these types of transplantation is recommended for them.
- High-risk AML: Allogeneic stem cell transplantation is generally recommended with first remission or partial 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 comorbidities.
- Autologous stem cell transplantation outside of a clinical-trial setting is not commonly used to treat AML.

Chronic lymphocytic leukemia (CLL)

- Allogeneic transplantation (usually reduced intensity but sometimes standard) is under study in clinical trials as treatment for patients whose CLL has certain high-risk features or whose disease has relapsed after standard therapies.

Chronic myeloid leukemia (CML)

- In cases of either advanced or refractory disease or intolerance to oral CML therapies, 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 is refractory to treatment or relapses after initial therapy.
- Standard and reduced-intensity allogeneic stem cell transplantation are under study in clinical trials as treatment for HL patients who have a suitable allogeneic donor.

Non-Hodgkin lymphoma (NHL)

- Autologous stem cell transplantation is generally used to treat patients with relapsed or refractory disease; transplantation during first remission is done only in clinical trials, except for certain types of NHL, including some cases of mantle cell lymphoma and T-cell lymphoma.
- Allogeneic transplantation is used to treat patients who have B-cell lymphoma (such as high-grade lymphoma, diffuse large B-cell lymphoma [DLBCL], follicular and mantle cell lymphoma), and is generally used for select cases after failure of autologous transplant and CAR T-cell therapy. Allogeneic transplantation is considered for first- and second-line treatment for peripheral T-cell lymphoma.
- Patients should check with their doctors to find out if there are specific recommendations for their subtype of NHL.

Myelodysplastic syndromes (MDSs)

- 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.

Myeloma

- Autologous stem cell transplantation is an important part of treatment for certain myeloma patients. The use of double autologous (tandem) transplants may also be used for some high-risk myeloma patients.
- Allogeneic stem cell transplantation is not commonly used for myeloma patients, but it may be a treatment option for selected younger patients who have a suitable allogeneic donor available.
- Reduced-intensity allogeneic stem cell transplantation is used in 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 patients who have high-risk features (such as mutations, etc.) and who also have a suitable allogeneic donor available
- Polycythemia vera (PV) and essential thrombocythemia (ET): Allogeneic stem cell transplantation and reduced-intensity allogeneic stem cell transplantation are occasionally used to treat these diseases.

Preparing for Transplantation

Medical Tests. Stem cell transplantation is a rigorous medical procedure. Before undergoing transplantation, patients will be given medical tests to ensure that they are healthy enough for the procedure. These tests may include:

Chest x-ray. A chest x-ray provides information about the size of the heart and lungs, and it may also detect the presence of infection or lung disease.

Pulmonary function test. A pulmonary function test is a breathing test used to measure how well the lungs are working.

Electrocardiogram (EKG). Electrodes (flat, sticky patches) are placed on the chest to evaluate the heart's rhythm.

Echocardiogram (ECHO). Using ultrasound waves to create a picture, an echocardiogram shows the size, shape, and position of the heart. The test also shows the parts inside the heart such as the valves and the motion of the heart while it is beating.

Blood tests. Blood tests are used to evaluate kidney and liver function, thyroid function, blood counts, and hemoglobin levels. These tests also show past exposure to certain infectious diseases, such as human immunodeficiency virus (HIV), hepatitis B and C, and cytomegalovirus (CMV). Blood tests also screen for other viral and bacterial infections.

Urine tests. Urine tests are used to measure kidney function.

Computed tomography (CT or CAT) scans. Computed tomography scans are x-rays that provide detailed images of the body, including soft tissue and bone.

Skeletal survey. A skeletal survey is a series of x-rays of major bones. It is used to check for any signs of disease and is usually done for patients with myeloma.

PET scan. A procedure in which a small amount of radioactive glucose (sugar) is injected into a vein, and a scanner is used to make detailed, computerized pictures of areas inside the body where the glucose is taken up. Because cancer cells often have more glucose than normal cells, the pictures can be used to find cancer cells in the body.

Bone marrow aspiration and biopsy. These tests are done to evaluate how well the bone marrow is producing blood cells and to check for any signs of cancer in the bone marrow. After a local anesthetic is given to numb the area, samples are taken from the patient's hip bone. Bone marrow has both a solid and liquid part. For a bone marrow aspiration, a special hollow biopsy needle is inserted through the hip bone and into the marrow to remove (aspirate) a liquid sample containing cells. For a bone marrow biopsy, a specialized wider needle is used and a sample of solid bone that contains marrow can be removed. These two tests are almost always done at the same doctor or hospital visit. **Visit www.LLS.org/3D to view an interactive 3D image which will help you visualize and better understand the bone marrow aspiration and biopsy procedures.**

Lumbar puncture. This is a procedure that is used to check for abnormal cells in the fluid that surrounds the brain and spinal cord called the "cerebrospinal fluid." A thin needle is inserted into the lower part of the spinal column and a small amount of cerebrospinal fluid is collected. A lumbar puncture is done only for certain types of leukemia and lymphoma.

Dental examination. A dental checkup is needed to ensure that any dental problems, such as cavities, loose fillings or gum disease, are resolved before the transplantation. **For more information, see the free LLS booklet *Dental and Oral Complications of Cancer Treatment*.**

Radiation oncology consultation. If radiation therapy is part of the conditioning treatment, patients meet with the radiation oncologist to go over the treatment plan. Patients also attend a simulation session during which many imaging scans are taken, along with measurements of the chest. This is done to create shields made of lead that will protect the lungs during radiation treatment.

Caregiver. It is important for patients preparing for transplantation to choose a caregiver or caregivers for help at home after their procedure. Patients who undergo stem cell transplantation will need an adult caregiver who will be responsible for some of the medical, emotional and daily support during recovery. Sometimes a caregiver is one person, but often several people can help at different times throughout the process. A caregiver can be a spouse, partner, sibling, parent, adult child, or a close friend. If you do not have a caregiver, speak with your medical team about possible alternatives. At least one caregiver should be with the patient at all times once the patient is discharged from the hospital, in case unexpected complications arise and help is needed. Members of the patient's healthcare team will teach the caregiver(s) the necessary skills to care for the patient.

Once the patient returns home, the caregiver will need to be prepared to help them by providing the following:

Medical Support. The caregiver(s) may need to:

- Ensure that the patient takes the correct dose of medication at the right time
- Notice any changes in the patient's condition
- Monitor the patient for new symptoms and immediately report them to the patient's medical team
  - Some conditions, such as infections and graft-versus-host disease (GVHD), need to be treated quickly. See *Graft-Versus-Host Disease* on page 35. The caregiver should be aware of symptoms and know the correct member of the healthcare team's phone number to call during office hours, at night and on weekends.
- Call for medical help in an emergency.

Emotional Support. The caregiver(s) should:

- Pay close attention to the patient's moods and feelings
- Listen to the patient and be supportive
- Keep family and friends informed about the patient's progress

Practical Support. The caregiver(s) should anticipate that it may be necessary for them to:

- Prepare meals and clean the house
- Provide transportation to medical appointments
  - After discharge from the hospital, patients will need to go to frequent medical appointments. The caregiver should plan to provide or arrange transportation and accompany the patient to the appointments.
- Assist with the patient's daily activities including, if necessary, caring for pets
- Assist with financial and insurance issues and help manage transplant costs

- Ensure that household bills are paid on time
- Manage the number of visitors and keep the patient away from anyone who is sick

Cost of Transplantation. Stem cell transplantation is an expensive procedure. As soon as a stem cell transplant is being considered as a treatment option, patients should discuss financial issues with their treatment team, including a licensed social worker. Some transplant centers also offer the services of a financial coordinator. This person can help patients understand what benefits are covered by their insurance and communicate with the insurance company if necessary.

Most insurance plans cover some of the costs of transplantation for certain cancers or diseases. Some insurance plans cover the transplant procedure but may not cover the costs of all the services a patient may need before or after the transplant. Before undergoing transplantation, patients should contact their medical insurance providers and determine which costs the insurance provider will cover. If the insurance company denies coverage for a recommended treatment, procedure, or prescription medication, patients may be able to get the decision overturned by filing an appeal with their insurance company. If claims are repeatedly denied, patients may want to contact their state's insurance agency or an attorney.

Patients in need of financial assistance should talk with their transplant teams about organizations that offer financial assistance to patients who qualify. Caregivers can also help patients find alternate sources of financial assistance.

In addition to medical bills, both patients and caregivers may need to plan for taking time away from work. Both patients and caregivers may be eligible to take unpaid, job-protected leave with continuation of group health insurance coverage under the Family and Medical Leave Act. Patients and caregivers should contact their workplace human resources department to see if they are eligible under this law.

Some patients may be eligible for Social Security Disability (SSD) benefits. The Social Security Administration (SSA) pays a monthly cash benefit to individuals who are unable to work (disabled) due to a severe medical condition that has either lasted, or is expected to last, at least one year. According to SSA guidelines, treatment with a stem cell transplant is considered a disability. To learn more about disability (SSD) benefits, patients can go to ssa.gov/disability or call (800) 772-1213. Many transplant patients receive SSD during their treatment and recovery and then once they can return to work, these social security disability benefits will be discontinued.

Some patients may receive disability insurance through their employers. Sometimes these disability plans are automatically offered as part of an employee's benefit plan. In other cases, the employee is required to purchase disability insurance. Patients should contact their human resources department to see whether they either have, or are eligible for, disability benefits.

Questions to ask the transplant center financial coordinator or the health insurance representative:

- **Does my insurance cover...**
  - A stem cell transplant for my disease?
  - The type of transplant my doctor has recommended (allogeneic, autologous, etc.)?
  - The cost of testing my family members (to find a match)?
  - The cost of testing to find an unrelated donor?
  - The collection of bone marrow from donor or cord blood units?
  - Additional costs (such as travel or lodging) for me or my caregiver?
  - The cost of prescription medicines needed before and after transplantation?
- **Are there any costs related to the transplant that are not covered?**
- **Are there any limits to what my insurance will pay, such as how many people can be tested to find a match?**

You can also contact an LLS Information Specialist at (800) 955-4572 for information about our Co-Pay Assistance Program and other financial assistance programs. For more information and resources to cope with the financial aspects of cancer care, please see the free LLS book *Cancer and Your Finances*.

Fertility. High doses of chemotherapy and radiation can affect cells in both male and female reproductive systems. Patients who have already received chemotherapy or radiation therapy prior to transplantation may or may not be fertile. Recovery from stem cell transplantation may take months to years, and patients of childbearing age may not be physically or psychologically ready to think about parenthood for several years after transplantation. Patients who want to have children in the future should discuss options to preserve fertility before transplantation.

- **Male fertility**—Males may consider preserving their fertility before transplantation by having their sperm collected and frozen for future use. The sperm will be collected before the conditioning regimen is started.
- **Female fertility**—Most female patients experience either temporary or permanent menopause as a side effect of transplantation. Females who are interested in trying to preserve their fertility should speak with their medical team and request a referral to a fertility specialist before starting treatment when possible.

One option for females is having their eggs frozen before treatment. Mature eggs are stimulated, removed and frozen, either unfertilized or fertilized with sperm. Another option is available for females who do not yet have mature eggs and for females who must start treatment immediately and who do not have time to undergo egg retrieval; they can have ovarian tissue removed (during an outpatient surgical procedure) and then frozen for future transplantation back into the body. The goal is preserving enough immature eggs to save female fertility.

For more information, see the free LLS booklet, *Fertility and Cancer*.

Insertion of a Central Venous Catheter. During the transplantation process, a patient will need to have many intravenous (administered directly into a vein) infusions. In addition to the infusion of stem cells, patients may also receive other infusions, including fluids, chemotherapy, antibiotics, other drugs and transfusions of red blood cells and platelets. Patients will also need to have blood drawn frequently for the testing required to monitor their progress. These injections, if given individually, would be painful and the veins in the hands and arms could not sustain so many frequent needle pricks. Therefore, prior to the transplantation, patients will have a central line (central venous catheter [CVC]) inserted if they do not already have one.

A CVC is a tube that is inserted through the skin into a large vein, usually in the upper chest. Placement is most often done when the patient is under local anesthesia. To place the CVC, a small incision is made where the catheter (tubing) enters the vein, and the catheter runs all the way to a large vein near the heart. Small, clear dressings are changed frequently to prevent infection. Having a CVC makes treatment more comfortable.

Depending on the frequency of later blood draws, the CVC may be changed to an implantable port or a peripherally inserted central catheter (PICC). A port is a two-part venous access device--a self-sealing portal and the catheter. It is surgically implanted under the patient's skin (see **Figure 1** on page 16). A port offers lower risk of infection and allows the patient more freedom in activities of daily living. A PICC line is a long tube inserted into a vein in the arm and passed through to the larger veins near the heart.

Port and Catheter

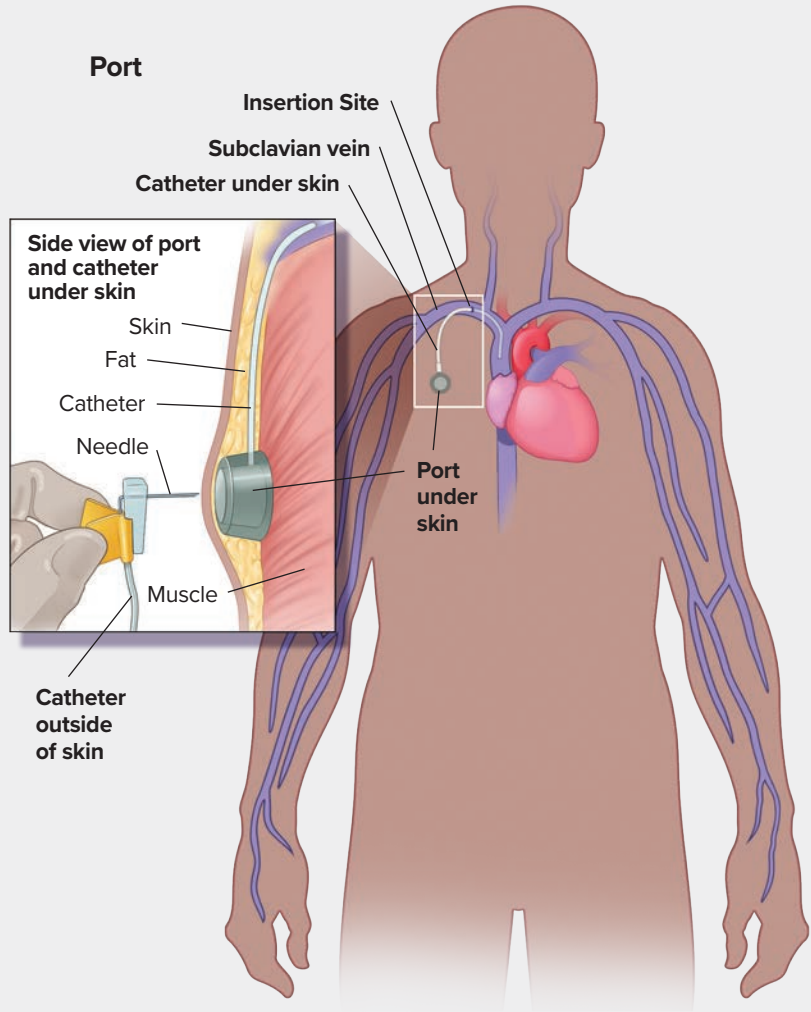

Figure 1. This picture shows where a port would be placed on the chest and how a member of the healthcare team would use the port to access the catheter under the skin, via the port.

Types of Stem Cell Transplantation

Depending on a patient's disease and health status, the doctor may recommend either an autologous or an allogeneic stem cell transplantation. The decision about which treatment to use is complex, and the factors that must be considered are different for each patient. Therefore, the decision should involve a thorough discussion between patient and doctor.

Autologous Stem Cell Transplantation. In autologous stem cell transplantation, the procedure uses the patient's own stem cells for the transplant (See **Figure 2** on page 18). The stem cells are collected from the patient's blood or bone marrow in advance and are frozen. The primary purpose of an autologous transplantation is to allow the patient to receive high doses of chemotherapy, either with or without radiation. This is called the "conditioning regimen." See *Conditioning* on page 30. These intensive, high-dose treatments usually destroy cancer cells better than standard treatments, but they can also destroy the blood-producing stem cells in the bone marrow. That is why the stem cells are removed before the treatment.

After the patient undergoes high doses of chemotherapy, either with or without radiation therapy, the stem cells are then returned to the body. The infusion of the patient's own healthy stem cells can restore the bone marrow's ability to make new blood cells and reestablish the patient's immune system. This is called "engraftment." Engraftment occurs more quickly in an autologous transplantation than in an allogeneic transplantation. The frozen cells are the patient's own stem cells, so graft failure (when the transplanted cells do not successfully grow and divide in the bone marrow) is rare, and graft-versus-host disease (GVHD) is never a problem. This type of transplant is often used to treat blood cancers such as Hodgkin lymphoma, non-Hodgkin lymphoma and myeloma.

Autologous transplantation, however, cannot produce what is called the "graft-versus-tumor" effect that patients may obtain from an allogeneic (donor) transplantation. As a result, there is a higher risk of relapse of the disease.

Most people will have a single autologous transplant. In select cases, others may have a transplant called a "tandem transplant." A tandem transplant involves a planned second autologous stem cell transplant after the first autologous transplant. All the stem cells are collected from the patient before the first-high dose chemotherapy treatment. After the first transplant, half of these stem cells are infused into the patient's body. Several weeks or months may pass before the second course of high-dose chemotherapy is given, after which the other half of the healthy stem cells that were originally removed are re-infused into the patient's body. This method is under study in clinical trials for the treatment of several types of cancer, including myeloma.

Autologous Stem Cell Transplantation

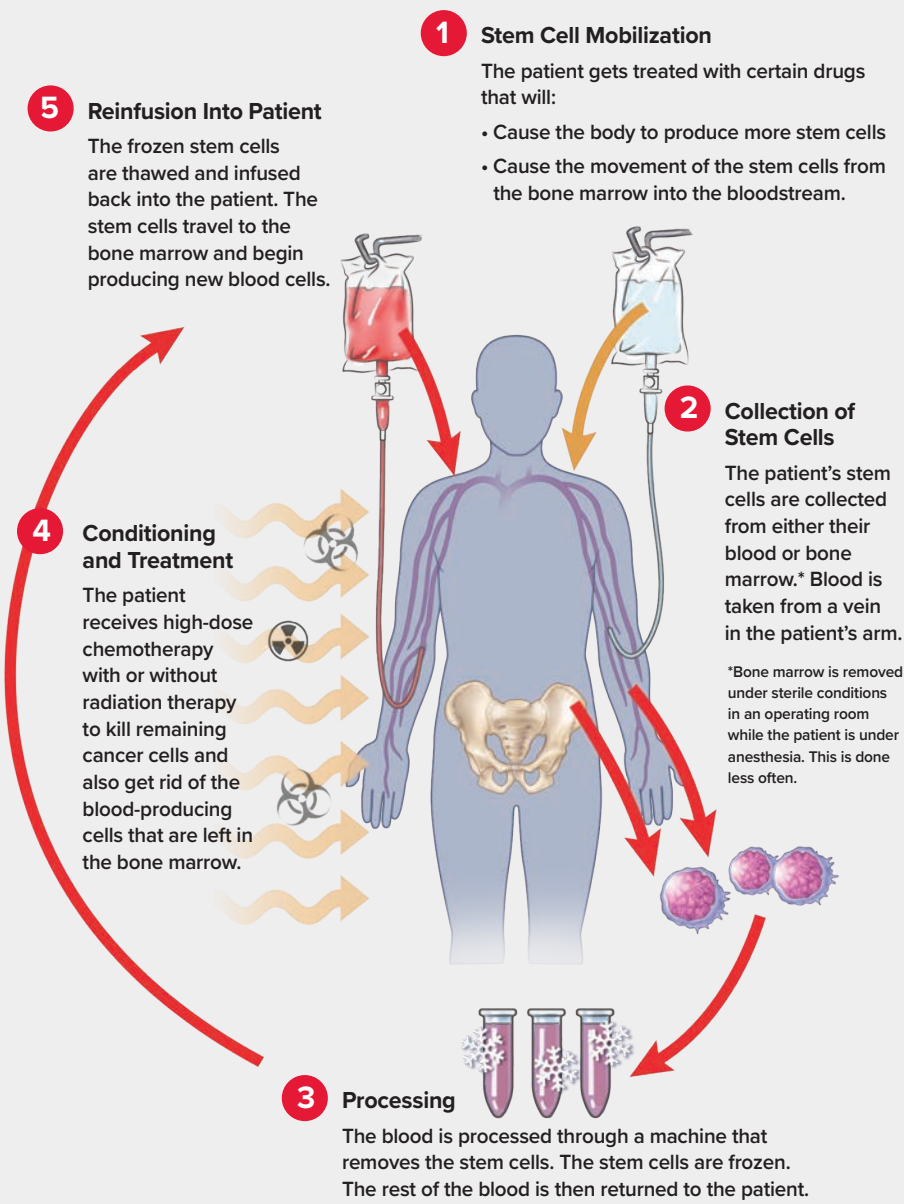

Figure 2. This illustration shows the autologous stem cell transplantation process. Once the stem cells are collected from the donor (patient), the cells are mixed with a cryoprotective agent so that they can be frozen (for many years) and then later thawed without injury. Once the patient has completed the conditioning treatment, the frozen stem cell collection is thawed and infused into the patient so that blood cell production can be restored.

Standard Allogeneic Stem Cell Transplantation. This type of transplantation involves the use of stem cells taken from someone (a donor) other than the patient. See **Figure 3** on page 20. The donated stem cells can come from either a related or an unrelated person. This type of transplant is often used to treat blood cancers such as chronic and acute leukemias, myelodysplastic syndrome, myeloproliferative neoplasms and myeloma.

Before an allogeneic stem cell transplantation, the patient receives a conditioning regimen of chemotherapy and sometimes radiation therapy. See *Conditioning* on page 30. This conditioning treatment is given to destroy any remaining cancer cells in the body. This helps weaken the patient's immune system to help keep the body from rejecting the donated cells after the transplant. It also allows the donor cells to move through the bloodstream to the bone marrow, where the donor cells will begin to grow and produce new blood cells, including red blood cells, platelets and white blood cells. This process is called "engraftment."

When a transplant is successful, the donor stem cells can replace stem cells in the bone marrow. It may also provide the only long-term cure for the patient's disease. One of the benefits of allogeneic stem cell transplantation is that after the donated cells engraft in the patient, they create a new immune system. The donated cells produce white blood cells that attack any remaining cancer cells in the patient's body. This is called the "graft-versus-tumor effect," and it may be even more important than the very intensive conditioning regimen that is administered to destroy the cancer cells. This benefit can only occur in allogeneic stem cell transplantation.

One complication of allogeneic transplantation is that the patient's body—despite the treatment to suppress the immune system—may reject the donated stem cells before they are able to engraft in the bone marrow. The patient's immune cells may see the donor's cells as foreign and destroy them.

Another complication of allogeneic transplantation is that the immune cells from the donor (the graft) may attack healthy cells in the patient's body (host). This is called "graft-versus-host disease" (GVHD). The parts of the body that are most often attacked by GVHD include the skin, intestines and liver; however, any organ can potentially be harmed. Graft-versus-host disease severity can range from mild to life-threatening. See *Graft-Versus-Host Disease* on page 35.

Reduced-Intensity Allogeneic Stem Cell Transplantation. Reduced-intensity allogeneic transplantation (sometimes called "mini-transplant" or "nonmyeloablative transplant") uses lower, less toxic doses of chemotherapy and radiation than the conditioning regimen given before standard allogeneic transplantations. This type of transplant may be an option for certain patients who are older, who have diseases that involve major organs, such as the heart or liver, or who are otherwise not healthy or strong enough to undergo standard allogeneic transplantation. With a reduced-intensity conditioning regimen, the patient's blood counts may not fall as low as they would with high-dose

Allogeneic Stem Cell Transplantation

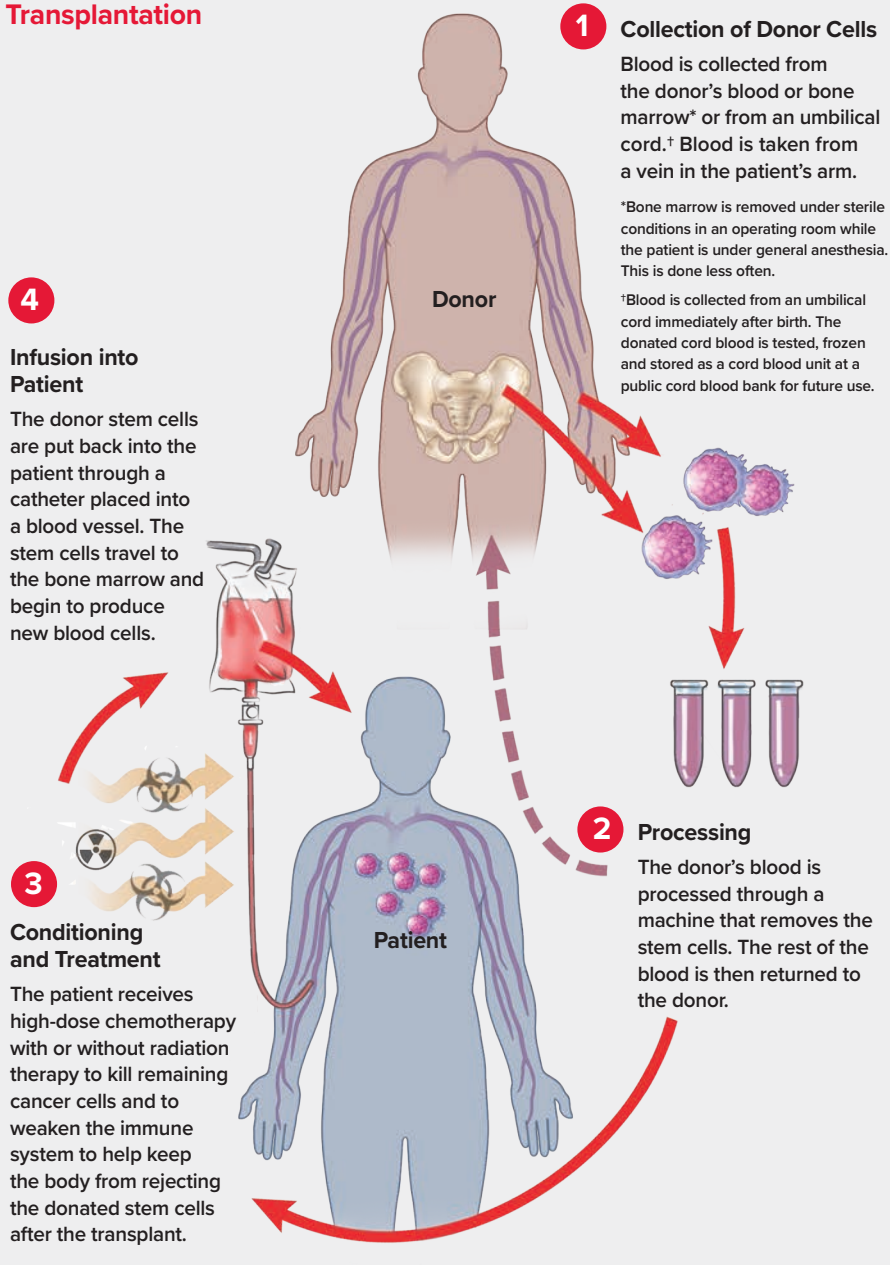

Figure 3. This illustration shows the allogeneic stem cell transplantation process. Once the stem cells are collected from the donor, the cells are mixed with a cryoprotective agent so that they can be frozen (for many years) and later once a patient is identified and the cells are needed, the cells can be thawed without injury and shipped to the patient.

chemotherapy. Additionally, the less toxic regimens put less strain on the patient's major organs, making this regimen more tolerable and safer. Sufficient numbers of reduced-intensity allogeneic stem cell transplants have been performed to determine that it may be an appropriate treatment for certain older, sicker patients who cannot tolerate a high-dose conditioning regimen.

The success of reduced-intensity transplantation depends on the graft-versus-tumor (GVT) effect of the donor stem cells, rather than on high-dose treatments to kill the cancer cells. The goal is to have the donor stem cells take up residence in the recipient's marrow and produce lymphocytes (white blood cells, part of the immune system) that will attack the patient's remaining cancer cells.

The conditioning regimen for a reduced-intensity allogeneic transplantation does not destroy as many cancer cells as the regimen for a standard allogeneic transplantation. But this conditioning regimen—along with potent drugs to suppress the patient's immune system—should weaken the patient's immune system enough so that it cannot attack and reject the donor cells, allowing the donor cells to take over the bone marrow and produce a new immune system to fight the cancer.

In some instances, blood cells from both the donor and the patient may exist in the patient's bone marrow for some time after transplantation. When the donor's immune system does not completely replace that of the patient (a state called "mixed chimerism"), the patient may be given an injection of the donor's lymphocytes (white blood cells) to improve engraftment and possibly the immune system's antitumor effects. This procedure is called a "donor lymphocyte infusion" (DLI).

Reduced-intensity allogeneic transplantations carry many of the same risks as standard allogeneic transplantations. One risk is that the patient's body may reject the donated stem cells before they are able to engraft in the bone marrow. The patient's immune cells may see the donor's cells as foreign and destroy them before engraftment can begin. Another risk is graft-versus-host disease (GVHD) (see *Graft-Versus-Host Disease* on page 35).

Research shows 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 (MDSs). The doctor will discuss with patients whether a reduced-intensity allogeneic transplant is an option for them.

Tissue Typing for Allogeneic Transplantation. Once it is determined that allogeneic stem cell transplantation is a treatment option for a patient, the patient's treatment team will begin to search for a suitable donor. For most patients, the success of allogeneic transplantation depends, in part, on how well the donor's tissue type matches the patient's tissue type. Historically, patients who are not well matched have high rates of graft failure and graft-versus-host disease, as well as very poor survival.

People have different sets of proteins or markers called “human leukocyte antigens” (HLAs) on the surface of most of their cells. The immune system uses these markers to identify which cells belong in the body and which cells do not. A person’s immune system knows which pattern of HLA markers are found in the body. If it finds a cell that has a different pattern of markers, it will attack and kill it.

HLA typing can be evaluated in two ways:

- A blood test
- A swab of the cheek

The findings determine how closely the tissue type of one person matches the tissue type of another person. A close match is important because it improves the chances of a successful transplant. The more markers two people share, the greater the chance that their immune systems will not view each other as foreign, and they will be less likely to attack each other. When the patient’s immune system is less likely to attack the donor cells, those new cells can engraft so they will grow and make new blood cells in the bone marrow. A closer match also reduces the risk of graft-versus-host disease (GVHD), a complication in which the donor cells attack the patient’s healthy cells (see *Graft-Versus-Host Disease* on page 35).

There are several HLA markers, but HLA typing is usually based on either 8, 10 or 12 HLA markers. When two people share the same HLA markers, they are a good match. In many transplant centers, doctors may require at least 6 or 7 of the 8 markers to match in order to perform the transplantation.

Individuals inherit half of their HLA markers from their mothers and half from their fathers, so most often the ideal donor is a patient’s sibling who has inherited the same HLA markers. On average, people have a one chance in four of having the same HLA type as their sibling, but many patients do not have a sibling with the same tissue type. Although an HLA-matched sibling is the preferred donor, only about 30 percent of patients have an available matched sibling donor.

For those patients without a matched family donor, an unrelated donor may be found through a volunteer donor registry. Donor registries are in place to identify an unrelated donor who has a tissue type that matches the patient’s tissue type. The *Be The Match* Registry®, operated by the National Marrow Donor Program® in partnership with international and cooperative registries, provides doctors with access to nearly 39 million potential donors and more than 806,000 cord blood units worldwide. Unfortunately, even with these large registries, well-matched HLA donors and cord blood units are not always available for patients. Therefore, researchers are studying ways to increase the pool of potential donors.

Cord Blood Transplantation. Cord blood is blood taken from the umbilical cords of newborn babies. Cord blood may be a viable alternative source of stem cells for patients without a well-matched related or unrelated donor. Unfortunately,

cord blood units tend to contain fewer stem cells and may be difficult to use in people with larger body sizes. In addition, this smaller cell dose and more immature immune cell system tends to be linked to longer times to engraftment and associated with higher risks of infection. Cord blood transplant patients also have an increased risk of graft failure. These problems may make these transplants more dangerous for some patients than for others. Cord blood, however, has a major advantage over matched unrelated donors; it is available much more quickly (potentially within 2 to 4 weeks) while it may take a month or more to obtain matched unrelated donor grafts. The time element is extremely important in high-risk blood cancers because the disease could relapse while the patient is waiting for a transplant. Exactly which donor type of transplant (matched, unrelated, cord blood or half-matched) leads to the best outcome for each type of blood cancer is still unclear and is an area of active investigation.

Another advantage of cord blood transplants is that cord blood may require a lower level of HLA matching between the donor and recipient. When compared with other transplants, those using the less mature stem cells from cord blood seem to be associated with a decreased risk of GVHD and therefore have a less strict matching criteria. For this reason, umbilical cord blood stem cell transplants may be considered when a well-matched donor cannot be found. This advantage of cord blood transplantation is particularly beneficial for patients from racial and ethnic minorities. According to a recent study from the National Marrow Donor Program, a well-matched unrelated donor was likely to be identified in 75% of patients of white European descent, while a donor was identified in the registry in only around 20% of patients with African ancestry and 35% of patients with Hispanic ancestry.

See the free LLS booklet *Cord Blood Stem Cell Transplantation Facts* for more information.

Mismatched Unrelated Donor Transplantation. Your doctor will try to match 10 to 12 HLA markers to lower the risk of graft-versus-host disease. In recent years, advances in medicine have allowed for the use of stem cell donors who are mismatched, meaning that not all 10 or 12 markers are a perfect match. Use of medications following transplant, such as cyclophosphamide (Cytoxan®), allow for mismatched donors while still lowering the risk of graft-versus-host disease.

Haploidentical Transplantation. To increase the number of potential donors for patients who cannot find a closely matched HLA donor, some transplant centers have begun to perform half-match (called “haploidentical”) transplant. In many cases a healthy, first-degree relative (a parent, sibling or child) can donate stem cells, even if they are only a half match. Since children receive half of their HLA markers from a parent, biological children and their parents will always be a half match, while there is a 50 percent chance of a sibling being a half match. Consequently, most individuals will have a suitable related haploidentical donor.

In addition to making it easier to find a suitable donor, the use of haploidentical stem cells is valuable because half-matched stem cells are often available much more quickly than a match from unrelated donor stem cells. Relatives may be able to donate on short notice, which may be less likely with an unrelated donor. This is important in cases when timing can be crucial, especially for a patient with a high-risk blood cancer who may have a disease relapse while waiting for transplantation.

However, if the patient and the donor are only half matched, the patient is at greater risk for graft failure and graft-versus-host disease (GVHD). To prevent these complications, the doctor will remove some of the T cells from the donor stem cells. Additionally, the drug cyclophosphamide (Cytoxan®) is administered shortly after the infusion of the stem cells to try to eliminate both some of the donor T cells (to prevent GVHD) and some of the recipient T cells and natural killer (NK) cells (to prevent graft rejection).

Although haploidentical transplant is starting to be used more frequently, it is still uncommon and not all transplant centers offer it. Nonetheless, researchers are studying this procedure as a viable option for increasing the number of potential donors for stem cell transplants with the hope that it can become a safer, more available option for patients.

Syngeneic Stem Cell Transplantation. This term is used to describe allogeneic transplantation when the donor and recipient are identical twins. Identical twins represent very few total births, so syngeneic transplantation is rare. Identical twins have the same genes and the same tissue type. With this kind of transplantation, donor cells are not rejected, and the patient's tissues are not attacked by the donor's immune cells. With identical twins, engraftment is usually associated with faster blood cell recovery and a quicker recovery of the immune system. No treatments are needed to prevent graft rejection or GVHD. The only disadvantage of a syngeneic stem cell transplant is that—just as with autologous transplantation— there is no graft-versus-tumor effect that would help to prevent a relapse of cancer.

Stem Cell Collection for Transplantation

Overview. There are three possible sources of stem cells for transplantation. They are:

- Peripheral blood
- Bone marrow
- Umbilical cord blood

The healthcare team will determine the appropriate source of stem cells, based on the patient's disease and health status. All donors are carefully screened to prevent any transmissible diseases and to detect other medical problems that might prevent the donor from providing stem cells. Remember that the donor may be the patient (autologous transplantation) or another person (allogeneic stem cell transplantation).

Peripheral Blood Stem Cell Collection. The stem cells used in peripheral blood transplantation are collected from the donor's bloodstream. Blood is the most common source of stem cells for both autologous and allogeneic stem cell transplantations. Collecting stem cells from the bloodstream is a nonsurgical procedure that involves less pain, no anesthesia, and no hospital stay, so it is easier on the donor than the more painful and complex procedure involved in removing stem cells from the bone marrow.

Another benefit of using a peripheral blood stem cell transplant is that after these cells are transplanted, they engraft and begin working more quickly than cells that are taken from the bone marrow. One major disadvantage of using peripheral blood stem cells, however, is that it is associated with a greater risk of graft-versus-host disease in allogeneic transplantations.

To obtain peripheral blood stem cells for transplantation, the donor will undergo the process of stem cell mobilization (to increase release of stem cells) and apheresis (collection of stem cells), described below.

Stem Cell Mobilization. Most stem cells are located in the bone marrow. Normally, the bone marrow releases only a small number of stem cells into the bloodstream. To obtain enough stem cells from peripheral blood for transplantation, the donor is given certain drugs that stimulate the release ("mobilization") of stem cells from the bone marrow into the blood. Starting 4 to 5 days before stem cell collection, the donor is given daily injections of drugs called "granulocyte-colony-stimulating-factors" (G-CSFs), such as filgrastim (Neupogen® or Zarxio®), lenograstim (Granocyte®), and pegfilgrastim (Neulasta®). Using G-CSFs greatly increases the chances of collecting enough stem cells for a transplant. Granulocyte-colony stimulating factors may cause some side effects for the donor, including bone and muscle aches, headaches, fatigue, nausea, vomiting, and/or difficulty sleeping. These side effects generally stop within 2 to 3 days of the last dose of the G-CSF medication.

In some cases, when the patient is the donor and the patient's own stem cells are used for the transplant (autologous transplant), the stem cells are mobilized by a combination of the chemotherapy that is used to treat the underlying disease and G-CSFs. In patients who have myeloma or non-Hodgkin lymphoma, the drug plerixafor (Mozobil®) may be given to mobilize stem cells for an autologous transplant in conjunction with filgrastim. Plerixafor may have additional side effects for the patient, including abdominal discomfort and diarrhea.

Apheresis. Once the stem cells are mobilized (released), they are collected from the blood of the patient/donor using a process called "apheresis." See **Figure 4** on page 27. The blood is removed from one of the donor's large veins (most likely from the arm) via a central venous catheter. The blood is then circulated through an apheresis machine, which separates the blood into four components: red blood cells, plasma, white blood cells, and platelets. The white blood cells are collected because they contain the stem cells. The rest of the blood is returned to the patient's/donor's body.

The number of stem cells that must be collected depends on both the patient's and the donor's weight as well as the disease for which the transplant is being performed. Stem cell collection is typically completed for an allogeneic transplant (from a donor other than the patient) after one or two sessions.

In autologous stem cell collections (where the blood is collected from the patient), if the patient has undergone prior chemotherapy, the collection of enough stem cells may require more than two apheresis sessions. When too few cells have been collected for an autologous transplantation, the patient may undergo treatment with either the same or different mobilization drugs. Then another attempt will be made to collect the necessary number of stem cells.

Apheresis usually takes 4 to 6 hours, does not require anesthesia, and usually causes minimal discomfort. Side effects for the patient/donor that may occur during the procedure include chills, lightheadedness, numbness around the lips, and cramping in the hands. Patients/donors typically tolerate apheresis well. During the procedure, an anticoagulant mixes with the patient's/donor's blood to keep it from clotting while it is circulating through the machine. The anticoagulant lowers the calcium level in the blood and this can occasionally cause sensations of coldness, numbness and tingling of the lips and fingers, and/or nausea. These side effects are temporary, but it is important for the patient/donor to let the apheresis technician or nurse know if they are having any of these symptoms during the procedure, as the patient/donor may need calcium.

For an allogeneic stem cell transplantation, if the stem cells are to be used immediately, they are placed in a plastic bag and, within a few hours, infused directly into the patient. If the donor is not located near the patient, the stem cells will be transported or they can be frozen and stored. For autologous transplantation, the patient's own stem cells will be frozen and then stored until they are infused.

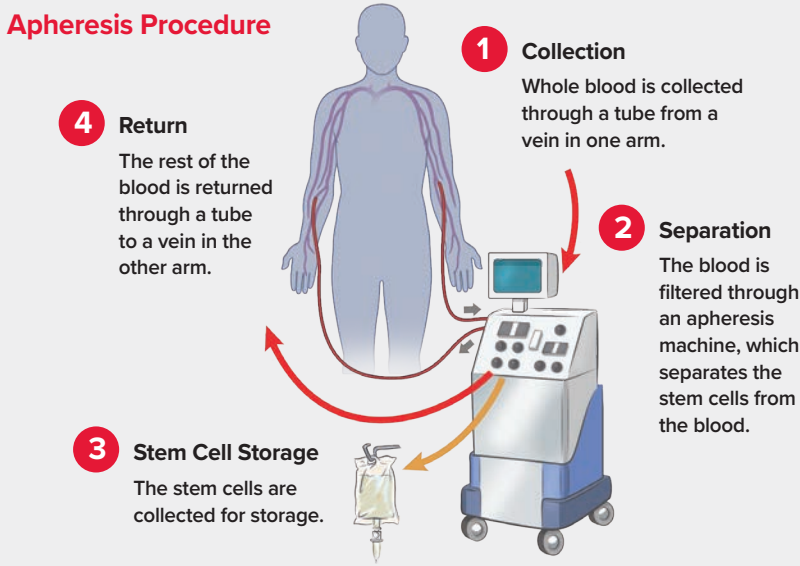

Figure 4. This illustration shows the apheresis process. This process is for a patient or a donor. This procedure may need to be repeated to obtain enough cells for the transplant. One or two collections may be enough to get the right amount of cells from allogeneic donors. For some patients getting an autologous transplant, three or more apheresis procedures may be needed.

Bone Marrow Aspiration. In certain situations, especially in allogeneic transplantations, stem cells harvested from the donor's bone marrow may be preferred, to lower the risk of graft-versus-host disease.

If stem cells are collected from the bone marrow, a procedure called "bone marrow aspiration" is done. Bone marrow donation is a surgical procedure and is performed in an operating room, using either regional or general anesthesia. The doctor uses a special hollow needle that is attached to a syringe. The needle is inserted through the patient's skin into one or more areas of the hip bone and the doctor withdraws bone marrow from the top edge of the hip bone of the donor. Several pints of marrow are removed. The donor usually remains in the hospital for about 6 to 8 hours, including recovery time. During this time, the donor recovers from both the anesthesia and the acute pain at the needle insertion sites. Typically, the donor can expect to feel soreness in the lower back, which will improve slowly over a few weeks or possibly longer. Most donors can return to their normal routine within a week. Side effects from the anesthesia for the donor may include nausea, headache and fatigue.

The donor stem cells are collected in a plastic blood transfusion bag. If stem cells are being retrieved from bone marrow, special filters are used to separate bone fragments, fatty particles, and large clusters of cells from the collected stem cells

before the rest of the collection is placed into the transfusion bag. This is done in the operating room or in the laboratory. The collection is then sent to either a blood bank or cell-processing laboratory where:

- The number of cells is determined
- Either the red blood cells or the plasma (the fluid surrounding the cells) may be removed if the donor and recipient do not share the same red blood cell type

The stem cells can be administered to the patient within 24 hours. If necessary, the harvested bone marrow cells can be frozen and stored for later use.

Visit www.LLS.org/3D to view an interactive 3D image which will help you visualize and better understand the bone marrow aspiration procedure.

Umbilical Cord Blood. The blood in a newborn baby's umbilical cord and the mother's placenta contains stem cells. This blood is 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 are collected, either before or after the placenta is delivered, depending on the procedure at the hospital. The cord and placenta blood are collected into a sterile bag; this bag of blood is the "cord blood unit." The cord blood unit 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 tissue typing to determine the level of matching to potential recipients, blood cell counts, and analysis for infectious agents such as human immunodeficiency virus (HIV), cytomegalovirus (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. When testing has been completed, the blood is frozen and stored at an extremely 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.

Table 2 (on page 29) summarizes the benefits and drawbacks associated with employing each of the different stem cell sources (bone marrow, peripheral blood and umbilical cord blood) for hematopoietic stem cell transplantation.

Comparison of Hematopoietic Stem Cell Sources for Transplantation

	Benefits		Drawbacks	
Stem Cell Source	**Donor**	**Recipient**	**Donor**	**Recipient**
Bone Marrow		• Lower risk of GVHD	• More invasive HSC collection • Possible discomfort and pain	• Close HLA matching required
Peripheral Blood	• No general anesthesia required for collection • Less discomfort and pain	• Faster engraftment and immune system reconstitution		• Higher risk of GVHD
Umbilical Cord Blood	• Non-invasive	• Lower risks of GVHD and relapse • Rapid availability • Less restrictive HLA matching		• Lower number of HSCs • Slower engraftment and immune system reconstitution

Table 2. Abbreviations: GVHD: graft-versus-host disease; HSC: hematopoietic stem cell; HLA: human leukocyte antigen; GVT: graft-versus-tumor effect.

Sources: 1. Adapted from Juric MK, Ghimire S, Ogonek J, et al. Milestones of hematopoietic stem cell transplantation–from first human studies to current developments. 2. Moore T. Hematopoietic stem cell transplantation (HSCT). Medscape [online]. *See References.*

Conditioning

"Conditioning" is a term used for therapy given to prepare patients for stem cell transplantation. Conditioning is usually a combination of two or more chemotherapy medications, either with or without radiation therapy. Remember, in an autologous transplant (when the patient's own stem cells are used for the transplantation) the stem cells are removed before the conditioning regimen begins.

Conditioning therapy is typically given over several days. Depending on the treatment plan, the number of days of conditioning will vary. Conditioning starts on a negative-numbered day (for example Day Minus 7 [Day –7, Day –6, etc.]). The day of transplant is counted as Day 0 (Day Zero). The days after the transplant are referred to as positive-numbered days (Day Plus One [Day +1, Day +2, etc.]).

The conditioning regimen:

- Treats the remaining cancer cells aggressively to make recurrence of the cancer less likely
- Inactivates the patient's immune system to minimize the chance of stem cell graft rejection in an allogeneic transplant
- Enables donor immune cells to engraft and exert their potent anti-tumor effects in allogeneic transplant

High-dose conditioning regimens are used for autologous stem cell transplantations and for a large percentage of allogeneic stem cell transplantations. This chemotherapy dosage is usually stronger than the doses received during earlier treatments. These high-dose regimens are particularly useful in treating patients who require stronger, more aggressive anticancer agents.

The conditioning that the patient receives is based on a number of factors, including:

- Type of cancer
- Source of stem cells
- Previous treatments

Certain conditioning regimens may cause difficult side effects, and members of the transplant team will discuss these with the patient before beginning the conditioning therapy. The chemotherapy will be given intravenously through the central venous catheter. During chemotherapy, the patient will receive intravenous fluids for hydration and medications, such as anti-nausea drugs, to ease uncomfortable symptoms. Patients who receive allogeneic stem cell transplants also start receiving immunosuppressant medication to prevent graft-versus-host disease.

Patients being prepared for a reduced-intensity allogeneic stem cell transplantation receive lower doses of chemotherapy drugs (either with or without radiation) in preparation for the transplant, compared with the dosages given to patients

receiving a standard allogeneic stem cell transplant. Medications are also given to suppress the immune system. The goal of this approach is to suppress the immune system enough to allow the donor stem cells to take over and produce a new immune system to fight the cancer.

Radiation Therapy. Radiation therapy given before transplantation is usually total body irradiation. Total body irradiation uses small doses of radiation delivered to the entire body, which can destroy cancer cells throughout the body. Total body irradiation therapy is administered in several divided daily doses. These divided doses minimize side effects such as lung injury, nausea and vomiting. The radiation treatments are usually given 1 to 3 times a day over 2 to 4 days immediately before transplantation. Having radiation therapy feels like having an x-ray and it does not hurt. However, there may be side effects after treatment.

An extra dose of radiation (called a boost) may be given to certain areas of the body. The treatment depends on the disease. For example, some men who have leukemia or lymphoma may receive a "boost" of radiation to their groin area to kill cancer cells that may be hidden in the testicles.

Rest. Some patients have a day or two of rest between their conditioning regimen and their stem cell infusion. The rest period gives the chemotherapy time to leave the patient's body so that when the patient receives the stem cells, there will be no trace of chemotherapy left in the body to harm the newly transplanted stem cells. Not all patients, however, have a day of rest between their conditioning regimen and transplantation.

Stem Cell Infusion

On Day 0 (Zero), transplant day, the stem cells that were collected are infused into the patient's bloodstream through the central venous catheter.

Infusing stem cells into the patient's vein is similar in many ways to administering a blood transfusion. For example:

- Prior to the transfusion, the patient receives intravenous fluids and medications to help prevent a reaction and reduce side effects during the infusion.
- 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. Often, patients experience no side effects from the infusion. If side effects do occur, they are treated and then the infusion is completed.
- When the stem cells have been collected and then frozen for storage, side effects are more common. The side effects are caused by the preservative used to store the stem cells. Side effects may include headache, nausea, flushing, and shortness of breath.

- Patients who receive stem cells that have been frozen and preserved may notice a strong, garlic-like taste in their mouths. Their urine and sweat may also have a garlic-like smell. (The smell is caused by the preservative used to store stem cells.) The smell will gradually fade over time, usually within a few days.

Some patients receive what is called a "T-cell depleted allogeneic stem cell transplant," in which the T cells are removed from the stem cells before they are infused into the patient. Elimination of T cells from the graft may reduce the risk of GVHD (graft-versus-host-disease). T-cell depletion, however, may lead to an increased risk of post-transplant infections, or even graft rejection and relapse. For these reasons, T cells are depleted from the stem cell collection only in certain circumstances.

Immediate Post-Transplant Period

After the stem cells are infused, they will travel to the bone marrow and make new blood cells. This is called "engraftment." Engraftment usually happens within the first 30 days after transplantation, but sometimes it can take longer. Engraftment means the new stem cells are working properly and starting to rebuild the immune system.

Engraftment marks the start of the recovery process. White blood cells are the first cells to engraft, followed by platelets and then red blood cells. The doctor will check the patient's blood counts every day to see if the patient's bone marrow has begun producing new blood cells. As engraftment occurs, the white blood cells, red blood cells and platelets will begin to increase in number.

Side Effects of the Conditioning Regimen. Prior to engraftment, blood counts will drop to their lowest levels and the patient's immune system will not be effective. At this point, the patient is at risk for infections as well as anemia (low red blood cell count), bleeding (low platelet count), and other concerns.

Infections. White blood cells, a part of the immune system, fight infections. During the post-transplant period, patients are very vulnerable to infections because they have very low white blood cell counts (a condition called "neutropenia"). Additionally, patients who have undergone allogeneic stem cell transplantation receive intensive treatments to suppress the immune system to prevent graft-versus-host disease. These immunosuppressive treatments further increase the risk of infections.

The patient's healthcare team will try to prevent and treat any infections that develop. Many precautions are taken to reduce the patient's risk of infection. For example:

- Patients receive broad-spectrum antibiotics, antiviral and antifungal agents to prevent infections.
- The cytomegalovirus (CMV) can cause serious complications and even death following transplantation. Cytomegalovirus is related to the viruses that cause chicken pox and infectious mononucleosis. Most adults in the United States

have been exposed to CMV. Once infected, a person carries the virus in an inactive state for life. A healthy immune system keeps the virus from multiplying and causing any further illness. Cytomegalovirus can, however, become a serious problem for people with weakened immune systems. It is possible for CMV to become reactivated after a stem cell transplant and cause a serious infection in any organ of the body.

Doctors may administer antiviral drugs to patients who test positive for CMV to try to prevent reactivation of the virus after transplantation. The US Food and Drug Administration (FDA) approved letermovir (Prevymis™), given by mouth or intravenous infusion, for prevention of cytomegalovirus (CMV) infection and disease in adults who may be susceptible to CMV infection after their stem cell transplant. Another approach is to give a patient regular blood tests after transplantation to check for early signs of CMV infection. If early detection finds traces of the virus, antiviral medication can be given to prevent it from spreading.

- Hand washing is very effective in reducing the spread of germs that cause infections. All visitors entering a patient's room should wash their hands.
- No visitors are allowed if they are sick. Patients should avoid close contact with anyone who has a cold, flu, chicken pox, measles or any other illness that can spread to the patient. Patients should also avoid contact with people who have had recent immunizations with live viruses.
- Plants and flowers should not be kept in the patient's room because they are potential sources of harmful microorganisms.
- Patients should minimize contact with pets and other animals while undergoing conditioning therapy.
- After transplantation, patients should receive a low-microbial diet comprised of foods that contain few potentially harmful microbes. Patients should avoid raw and undercooked meat and fish, non-pasteurized dairy products, raw eggs, raw honey, and unwashed raw vegetables and fruit.
- Patients should continue to follow the recommendations mentioned above even after they are discharged from the hospital, because it takes time for the immune system to recover. They should speak to members of their treatment team for specific recommendations about an appropriate diet or ask for a referral to a dietitian.

LLS Information Specialists, at (800) 955-4572, will also schedule a free consultation with a registered dietitian with experience in oncology nutrition.

Anemia. Low red blood cell counts can result in a condition called "anemia." Patients with anemia may experience weakness, fatigue, and shortness of breath. Transfusions of red blood cells can ease symptoms until the bone marrow begins to produce enough red blood cells. In certain cases where there is a mismatch in blood type, this process can take several months.

Thrombocytopenia. Thrombocytopenia is a condition in which there is a lower-than-normal number of platelets in the blood. After transplantation, platelet counts will be low. This low number of platelets may result in easy bruising and excessive bleeding from wounds or bleeding from mucous membranes such as the nose, mouth, skin and gastrointestinal tract. Certain activities should be avoided when platelets are low. Patients will receive platelet transfusions if their platelet counts are too low. Refer to your healthcare team's recommendations.

Side Effects on Organs and Body Parts. In addition to low blood counts, there are other short-term side effects associated with the conditioning regimen. The chemotherapy dosages used before transplantation are generally higher than the dosages used in standard chemotherapy, so the typical side effects of the conditioning-regimen chemotherapy may be more intense, especially during the weeks after transplantation. It is important for patients to notify their doctor or nurse of any side effects so they can be treated. The following areas of the body are especially sensitive to chemotherapy drugs and radiation therapy:

- **Gastrointestinal Tract.** Chemotherapy drugs can cause severe nausea and vomiting. Doctors often give anti-nausea medication along with chemotherapy to try to prevent this side effect. It is easier to prevent nausea and vomiting before it starts. Patients should inform their doctor or nurse how well these medicines are working to control their nausea and vomiting. If the medicines are not working, they may need to be changed. Patients may also experience diarrhea, intestinal cramps, and rectal or anal ulceration.
- **Mouth.** Another serious side effect is oral mucositis (mouth sores). These painful mouth sores can prevent patients from eating and drinking. When needed, an agent such as the epidermal growth factor palifermin (Kepivance®), given intravenously, can be used to prevent or minimize the effects of oral mucositis. Palifermin stimulates the cells that line the mouth (and gastrointestinal tract) to grow and develop.
- **Heart.** Some conditioning therapies can affect the heart. The effect may be temporary, but it can sometimes be permanent. Although damage to the heart is very serious, it is a rare complication.
- **Lungs.** One reaction that can occur because of intensive chemotherapy, especially when accompanied by total body irradiation, is called "interstitial pneumonitis," an inflammation in the lungs. Patients typically experience a dry nonproductive cough or shortness of breath. This side effect can be very severe and can also prevent the efficient exchange of oxygen in the lungs. 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. It is important for patients who experience shortness of breath or a new cough after transplantation to bring it to the immediate attention of their doctor or nurse, because interstitial pneumonia can be a serious or even fatal complication.

- **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 because 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, causing a condition called "edema" (swelling caused by too much fluid trapped in the body's tissues). In the lungs, fluid accumulation may cause congestion, poor exchange of oxygen and shortness of breath. Medications such as corticosteroids, which decrease inflammation, are sometimes used to manage this complication. Chemotherapy can also damage the patient's veins, leading to blood clots forming in the lower extremities. Many centers now give blood thinners to patients to reduce the chance of clots forming. Being out of bed and walking can also help reduce the likelihood of blood clots. Diseases, such as myeloma, also put the patient at higher risk of blood vessel issues.
- **Liver.** High-dose chemotherapy can result in damage to the liver. The blood vessels that lead into and pass through the liver are prone to becoming blocked after transplantation. Veno-occlusive disease (VOD), also known as "sinusoidal obstructive syndrome," causes the blood vessels that carry blood through the liver to become obstructed. Symptoms of VOD include jaundice (yellowing of the skin and eyes), weight gain (from fluid retention), and a painfully enlarged liver. VOD varies in severity. Sometimes it is mild and resolves quickly. Other times, VOD can be more serious, even life-threatening. Treatment of VOD may include red blood cell transfusions, diuretics and drug therapy. The Food and Drug Administration (FDA) has approved defibrotide sodium (Defitelio®) for the treatment of adult and pediatric patients with VOD who have renal or pulmonary dysfunction following stem cell transplantation.
- **Hair.** Hair loss can occur wherever there is hair on the body. It is generally temporary, and hair growth resumes when the regimen is discontinued. As hair grows back, it is important to keep the scalp, or other part of the body, protected from the sun, heat and cold. New hair may be a different color or texture than it was and it may be thinner than it was before the transplant.
- **Eyes.** The patient's eyes may become jaundiced (yellowed) or develop cataracts.

Graft-Versus-Host Disease

Graft-versus-host disease (GVHD) is a potentially serious complication of standard allogeneic and reduced-intensity allogeneic stem cell transplantations. GVHD occurs when the donor's T cells (the graft) view the patient's healthy cells (the host) as foreign, and attack and damage them. Graft-versus-host disease can be mild, moderate or severe. In some cases, it can be life-threatening. Patients should follow their treatment team's recommendations to increase their chance of a

better outcome. Risk factors for GVHD include:

- **Mismatched or not fully matched donor.** A close HLA match between donor and recipient helps lower the risk of GVHD but does not eliminate it.
- **Unrelated donor.** The risk for GVHD increases if the donor is not related to the recipient, even if they are a perfect HLA match.
- **Age (donor or recipient).** GVHD risk increases with age.
- **Female donor to male recipient.** This increases the risk of both acute and chronic GVHD.
- **Donor lymphocyte infusion.** When lymphocytes from a donor are given to a patient who has already received a stem cell transplant from that same donor, the risk for GVHD is increased.
- **Previously having had acute GVHD.** If a patient had acute GVHD previously, the risk of recurrent acute or chronic GVHD increases.

Unless the patient's donor is an identical twin, a patient receiving an allogeneic stem cell transplant will receive GVHD prevention. This may include removing T cells from the donor graft and/or giving medications to suppress the T cells in the graft so that they do not attack the patient's cells.

There is no standard regimen for the prevention of GVHD, and different combinations of medications are given at different institutions. Some of the medications used to prevent GVHD may also be used to treat it. These include:

- **Calcineurin inhibitors,** which suppress enzymes that activate the immune system:
  - Cyclosporine (Neoral®) – IV infusion, oral administration
  - Tacrolimus (Prograf®) – IV infusion, oral administration
- **Immunosuppressants** that lower the body's immune response:
  - Mycophenolate mofetil (CellCept®) – taken by mouth (orally)
  - Hydroxychloroquine (Plaquenil®) – taken by mouth
  - Sirolimus (Rapamune®) – taken by mouth
- **Corticosteroids** that weaken the body's immune response and reduce inflammation:
  - Methylprednisolone or prednisone – IV infusion or oral administration
- **Biologics** that stop or slow inflammation:
  - Abatecept (Orencia®) – IV infusion – Abatecept is indicated to be used in adults and pediatric patients two years of age and older undergoing hematopoietic stem cell transplantation from an unrelated donor, in combination with a calcineurin inhibitor and methotrexate.
  - Antithymocyte globulin (ATG) – IV infusion

- Alemtuzumab (Campath®) – IV infusion
- Tocilizumab (Actemra®) – IV infusion

- **Chemotherapy drugs** that eliminate certain donor T cells to help prevent GVHD:
  - Cyclophosphamide (Cytoxan®) – IV infusion
  - Methotrexate (Trexall®) – IV infusion, oral administration

Types of Graft-Versus-Host Disease. There are two main categories of GVHD: acute graft-versus-host disease and chronic graft-versus-host disease. Each type affects different organs and tissues and has unique signs and symptoms. Patients may develop one type, both types, or neither type.

Acute GVHD. This usually develops within the first 100 days after transplantation, but it can occur later. It affects between 30% and 70% of all stem cell transplant patients. Acute GVHD can affect the skin, the gastrointestinal tract or the liver. Symptoms may include:

- Rash, with burning and redness of the skin
  - This may erupt on the patient's palms or the soles of the feet, and 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, loss of appetite and diarrhea, which indicate involvement of the gastrointestinal tract
- Jaundice (yellowing of the skin or eyes), indicating that GVHD has injured the liver
  - Abnormalities of liver function would be noticed on blood test results.

Acute GVHD is given a stage (from 1 to 4) used to identify the extent of disease at the time of diagnosis. Each organ is staged individually. The skin is given a stage based on the amount of body surface area involved. The gastrointestinal tract is staged based on the amount of diarrhea or bowel movements a patient has per day. The liver is given a stage based on the rise in bilirubin level.

Many patients who develop acute GVHD in stage 1 are successfully treated with non-systemic therapy, including topical steroid creams to treat the skin. Treatment for acute GVHD in stages 2 through 4 may include:

- Continuation or restart of a previously used immunosuppressive agent
- Systemic steroids with or without topical steroids
- Sirolimus (an immunosuppressive drug used to prevent organ transplant rejection)
- Participation in a clinical trial

Extracorporeal photopheresis (ECP) is sometimes used to treat acute GVHD. In this procedure, the patient's blood is circulated outside the body through a machine that filters it. The filter separates the white blood cells from the rest of the blood. The white blood cells are combined with a light-sensitive agent called 8-methoxypsoralen and then exposed to ultraviolet A (UVA) light to activate the medicine, which kills the immune cells. The treated cells are then returned to the patient's body.

Ruxolitinib (Jakafi®), a medication taken by mouth, is FDA-approved to treat adult or pediatric patients 12 years and older with acute GVHD, as a second-line treatment after therapy with steroids has failed.

Chronic GVHD. This is a syndrome that may involve a single organ or possibly many organs. It is one of the leading causes of medical problems and death after an allogeneic stem cell transplantation and it affects approximately 40% to 50% of patients. Chronic GVHD may occur at any time after transplantation, but it typically occurs at least 100 days after the day of transplant.

Symptoms may be in the following places in the body:

Mouth. Symptoms may include:

- A very dry mouth
- Sensitivity to hot, cold, spicy and acidic foods; mint (eg, mint-flavored toothpaste); carbonated drinks
- Painful mouth ulcers that may extend down the throat
- Difficulty opening the mouth, and difficulty drinking or eating
- Gum disease and tooth decay

Eyes. Symptoms may include:

- Dry eyes
- Irritation that does not go away
- Blurred vision
- Teary eyes

Skin. Symptoms may include:

- A rash
- Dry, tight, itchy skin
- Thickening and tightening of the skin, which may result in restriction of joint movement
- A change in skin color
- Intolerance to temperature changes due to damaged sweat glands

Nails. Symptoms may include:

- Changes in nail texture
- Hard, brittle nails
- Nail loss

Scalp and Body Hair. Symptoms may include:

- Loss of hair on the head
- Premature gray hair
- Loss of body hair

Gastrointestinal Tract. Symptoms may include:

- Loss of appetite
- Unexplained weight loss
- Nausea
- Vomiting
- Diarrhea
- Stomach pain or cramping

Lungs. Symptoms may include:

- Shortness of breath and difficulty breathing
- A persistent, chronic cough that does not go away
- Wheezing

Liver. Symptoms may include:

- Abdominal swelling
- Jaundice (yellow discoloration of the skin and/or eyes)
- Abnormal liver function test results

Muscles and Joints. Symptoms may include:

- Muscle weakness and cramps
- Joint stiffness causing difficult full extension of fingers, wrists, elbows, knees, ankles

Genitalia. Symptoms may include:

- Female
  - Vaginal dryness, itching and pain
  - Vaginal ulcerations and scarring
  - Narrowing of the vagina
  - Difficult /painful intercourse

- Male
  - Narrowing and/or scarring of the urethra
  - Itching or scarring on the penis and scrotum
  - Irritation of the penis

See *Sexual Health* on page 44.

The type of care administered in the treatment of chronic GVHD depends on the organ(s) or site(s) affected; therapies used to treat chronic GVHD may be topical or systemic. Systemic treatment travels through the bloodstream and reaches cells throughout the entire body. Patients with mild symptoms of chronic GVHD, especially if the symptoms are limited to a single organ or site, can often be treated with close observation or with local/topical therapies. For example, mild cases of chronic skin GVHD may be treated with topical steroid ointments and cases of chronic ocular (eye) GVHD may be treated with immuno-suppressive eye drops.

Patients with more severe symptoms of GVHD or multi-organ involvement typically require systemic treatment. Prednisone is the standard first-line therapy for chronic GVHD. About 50% to 60% of patients with chronic GVHD will require a second-line treatment within two years. For patients who do not respond to prednisone or other steroid treatments, the Food and Drug Administration (FDA) has approved:

- **Ibrutinib (Imbruvica®),** taken by mouth, to treat adult and pediatric patients age 1 year and older with chronic GVHD after failure of one or more lines of systemic therapy
- **Ruxolitinib (Jakafi®),** administered orally, to treat adult or pediatric patients 12 years and older with chronic GVHD after one or two lines of systemic therapy have failed
- **Belumosudil (Rezurock®),** taken by mouth, to treat adult and pediatric patients 12 years and older with chronic GVHD after failure of at least two prior lines of systemic therapy

Other combinations of immuno-suppressive drugs may be used to control the symptoms of GVHD. **Patients must be aware of the warning signs of GVHD and should call their doctor immediately if they have any symptoms. Early detection and treatment may help limit the severity of the disease.**

For more information, see the free LLS booklet, *Graft-Versus-Host Disease*.

Graft Failure

Graft failure occurs when the transplanted stem cells (the graft) fail to move into the bone marrow and make new blood cells. Graft failure is extremely rare in autologous stem cell transplantation. In allogeneic stem cell transplantation, graft failure is more common when the patient and donor are not well matched, when the

patient receives a T-cell depleted transplant, and if the patient has a diagnosis of myelofibrosis. It can also occur in patients who receive a graft that has too few stem cells, such as a single umbilical cord unit. The risk of graft rejection lasts about 2 to 4 weeks after a transplant, but sometimes graft failure can happen even later.

The most common treatment for graft failure is a second transplant, either using stem cells from the same donor or from a different donor. Other treatment options may include donor lymphocyte infusion, or treatment within the setting of a clinical trial.

Post-Transplant Lymphoproliferative Disorders

Post-transplant lymphoproliferative disorders (PTLDs) comprise a group of rare disorders that cause out-of-control growth of lymphocytes (a type of white blood cell) after allogeneic stem cell transplantation. Most PTLDs are caused by the Epstein-Barr virus (EBV), a type of herpes virus. Generally, PTLD occurs within the first year after transplantation.

There is no standard treatment for PTLDs. Treatment for a PTLD depends on its subtype; however, reduction of immunosuppression medication is often the initial treatment approach for all subtypes. Reducing the dosage of immunosuppression drugs may allow the patient's own immune system to fight the EBV. Other treatment options include using the drug rituximab (Rituxan®) to kill the B cells, lymphocyte transfusions to boost the immune system, antiviral drugs to treat EBV infection, infusion of cytotoxic T lymphocytes, and/or a clinical trial. A treatment option for patients with a PTLD that is localized in one area of the body is surgical removal of the lymph node or tumor. Combination chemotherapy is a treatment option for patients with aggressive disease.

For more information, see the free LLS booklet, *Post-Transplant Lymphoproliferative Disorder.*

Early Recovery (From discharge up to about one year)

Once engraftment has occurred and early side effects or complications have been resolved, members of the transplant team will begin the process of discharging the patient. A patient is ready for discharge from the hospital or treatment center when:

- White blood cell engraftment has occurred, and the patient is producing enough neutrophils.
- There is no indication of infection.
- The patient can tolerate oral medications.
- The patient can eat and drink to get sufficient fluids and nourishment.
- There are no severe treatment complications.
- The patient is medically stable and physically able to function outside the hospital.

Although the patient's blood counts may be improving, the immune system is still very immature. Patients or their caregivers should call the doctor or nurse immediately if there are any symptoms of infection, including:

- Fever, flushing (red/pink skin), sweating or chills
- Coughing, sneezing, runny nose, sore throat or shortness of breath
- Nausea, vomiting or diarrhea
- Blurred vision or changes in the ability to see clearly
- Blood in the urine or pain during urination
- Rash or cold sores
- Irritation in the rectum, including burning and pain
- Small blisters around the mouth or on any other part of the body

Follow-up care is extremely important. It's crucial for the patient to attend regular appointments at the outpatient clinic and the doctor's office, as well as to be available for scheduled home care visits from professional healthcare personnel. Initially, doctor visits may be frequent, and allogeneic transplant patients may need follow-up visits several times a week. If all is going as anticipated, the patient's central venous catheter can be removed, and the frequency of follow-up visits can gradually be decreased. At these follow-up visits to the doctor's office or the outpatient clinic, the doctor will order blood tests to check blood counts, electrolyte levels, and liver and kidney function. During some visits, bone marrow aspirations and biopsies will be done to check blood cell growth in the bone marrow.

In general, there is a shorter recovery period after autologous stem cell transplantation than after allogeneic stem cell transplantation. In an autologous transplant, it often takes the immune system 3 to 12 months to recover. For an allogeneic transplant, it often takes at least 6 to 12 months to recover to nearly normal blood cell levels and longer for immune cell function. Immune system recovery can take even longer if the patient has GVHD and requires additional GVHD therapy.

The recovery time a stem cell transplant recipient needs before they feel "normal" or return to work or school is different for each person. For some patients, recovery after stem cell transplantation can be very difficult. It depends on a patient's side effects and complications.

During the recovery period, the patient's stem cells are creating new blood cells, and the cells in the mouth, stomach, intestines, hair, and muscles are regrowing. The body is exerting energy to make these new cells, and fatigue and weakness are not unusual. For most people, the first few months to one year after transplant remain a time of recovery. As patients regain strength, they may begin slowly resuming daily activities.

Immunizations. After transplantation, patients lose the protection from the vaccines that they received as children. All transplant patients need to receive childhood vaccines again once their immune systems have recovered. Autologous transplant recipients typically receive inactivated vaccines starting 6 months after transplant and live vaccines 24 months after transplant. For patients who have undergone allogeneic transplants, doctors may wait until 12 months after transplantation to start vaccinating patients, or until patients are off immunosuppressive therapy. Patients should follow their transplant doctor's recommended schedule for vaccinations.

Nutrition. In the recovery phase after stem cell transplantation, it is important to eat a well-balanced diet. After patients undergo chemotherapy and radiation treatment, their cells need to recover and repair themselves. Protein from food provides energy for the body and the building blocks for that repair. If a patient does not get the necessary number of calories and enough protein, the body may take the energy it needs from the muscles, causing further weakness and fatigue. Patients taking corticosteroids may have problems with sugar control and therefore should limit their carbohydrate consumption. Electrolytes, which are important minerals in the blood and other body fluids, can be obtained from certain foods and liquids, such as Gatorade. If a patient's food and drink intake is lacking or inappropriate, consultation with a dietician is important.

Reach out to LLS Information Specialists, at (800) 955-4572, to schedule a free consultation with a registered dietitian. Also, see the free LLS booklets *Nutrition* and *Food and Nutrition Facts*.

Personal Care. While recovering from transplantation, it's important to follow the guidelines listed below regarding personal care and hygiene:

- Shower or bathe every day but use mild soap and shampoo. Apply baby oil or a skin moisturizer while the skin is still damp.
- Limit time in direct sunlight. After transplant, skin can be more sensitive and may burn more easily. Protect the skin with sunscreen that has an SPF of at least 30. Wear protective clothing and a hat if you're expecting to be in direct sunlight for 20 minutes or longer.
- Do not get a manicure or pedicure in a nail salon while recovering from transplant. Have, or do one yourself at home, using your own equipment and tools.
- Do not re-use old makeup. Buy all new products after your transplant to reduce the risk of skin infections.
- Have dental check-ups every six months. Brush your teeth, gums and tongue after meals and before bed. Use toothpaste with fluoride and an alcohol-free mouthwash. Floss your teeth gently every day. Clean, brush and rinse dentures after meals and make sure dentures fit well.

Exercise. Most people find that it takes time to regain their strength. It may be helpful to follow a regular exercise plan. A growing body of evidence suggests that physical activities, such as walking, riding a stationary bicycle, yoga, tai chi, swimming or water exercises, and strength training may alleviate fatigue and increase energy levels. Patients should consult with their healthcare team before starting an exercise program. The healthcare team may refer patients to a physical therapist for an evaluation and an exercise plan.

Returning to Work and School. Typically, the earliest a patient can return to school or work is about 4 months after an autologous transplant and 1 year after an allogeneic transplant. This timeframe can vary from person to person and depends on the patient's health and type of work. If the work is either physically demanding or if it puts the patient at risk of infection, they may need to wait longer before returning to work. Going back to work or school gradually may be a good plan. For example, patients may want to return to work part-time at first, and then gradually increase their hours.

Making the transition back to school or work can be difficult. Some patients do not have the same stamina they had before transplantation and cannot keep up their former pace. Patients should talk to members of their transplant team about going back to school or work.

Sexual Health. After transplantation, patients often have difficulty engaging in sexual activity. This is caused by the physical effects of chemotherapy and radiation treatments. Common concerns include fatigue, loss of sexual desire, vaginal dryness, and getting and maintaining an erection. These concerns are often temporary and will likely be resolved over time. However, intervention may be needed to make patients feel more comfortable about sex. While some patients may feel awkward discussing these matters, it is important for patients and their partners to have answers to all their questions. Patients are encouraged to find someone on their transplant team with whom they feel friendly enough to discuss their concerns. There are medical and psychological interventions that are available to help patients.

Once patients feel ready to resume sexual activity, they need to take the following precautions to protect themselves:

- Avoid sexual activity that involves penetration or contact with mucous membranes until their white blood cell and platelet counts have recovered. This includes vaginal, oral and anal sex.
- Use latex condoms each time there is sexual activity even after white blood cell and platelet counts have recovered.
- Use a barrier device (condoms or dental dams) any time a partner's vaginal secretions or semen could enter the mouth.
- Avoid sex that involves contact with mucous membranes if a partner has a genital infection.

For more information, see the free LLS booklet, *Sexual Health and Intimacy*.

Survivorship (One year after transplant and beyond)

Long-term follow-up care is important after both autologous and allogeneic transplantation. Even after cancer treatment has ended, patients need to continue to schedule appointments with their cancer team in addition to having routine check-ups and health screenings. If patients are unable to return to the transplant center for yearly follow-up visits, it is important that their local oncologist be made aware of all the follow-up recommendations related to various organ systems. Long-term follow-up appointments and tests will typically continue for any number of years.

Long-Term Complications. Many transplant recipients experience the following long-term side effects even years after transplantation:

- Organ complications after transplant. There may be damage to the liver, kidneys, heart or lungs. Blood tests and pulmonary function tests will be done to monitor the patient's health. Stem cell transplant recipients have a higher risk of cardiac problems after transplant. Electrocardiograms and echocardiograms may be done to monitor new symptoms.
- The endocrine system—which makes hormones that control growth, sexual development, sleep, hunger and metabolism—may be affected by the transplant. Hormone levels, including thyroid levels, may not return to normal after a transplant. Some patients develop hypothyroidism (an underactive thyroid gland) after radiation therapy. If a patient develops hypothyroidism, the patient will receive oral thyroid medication.
  - Children may have a slowed growth rate and may require growth hormone treatments and replacement of other hormones.
  - In young patients, puberty may be delayed, and hormonal therapy required.
- Risk for bone loss and subsequent osteoporosis to long-term survivors of stem cell transplants. To reduce bone-fracture risk, patients may be advised to take adequate amounts of calcium and vitamin D. Patients at high risk for bone loss may be prescribed medications for the prevention or treatment of osteoporosis.
- Cataracts, caused by radiation therapy or high-dose steroids. After transplantation, patients should have their eyes regularly examined. Cataracts cause the lenses of the eyes to become cloudy and can occur in either one or both eyes. Symptoms include blurred, cloudy, or double vision; sensitivity to light; and difficulty seeing at night. Without treatment, cataracts can lead to blindness.
- Infertility. Chemotherapy and radiation treatments may lead to infertility. Hormone replacement is usually not necessary for males. For females, estrogen and progesterone replacement therapy may be needed. When pregnancy is not desired, the use of contraception is recommended because it cannot be predicted when, or even if, fertility will return.

- Chronic GVHD. A potential late complication of stem cell transplantation. GVHD can affect any part of the body. Severe chronic GVHD can negatively affect a patient's health and quality of life. Patients should be aware of the warning signs of chronic GVHD and should call their doctors immediately if they have any symptoms. Early detection and treatment may help limit the severity of the disease. See *Chronic GVHD* on page 38.

- Feelings of depression and anxiety are common during this time. Patients should seek medical advice if their mood does not improve over time—for example, if the patient feels depressed every day for a two-week period. It may be helpful for the patient to get a referral to a therapist or counselor who has experience treating people who are recovering from life-threatening illnesses.

- Risk for relapse. After transplantation, the cancer may return (relapse). Learning of a relapse can be distressing and overwhelming, but it is important to remember that there are other treatment options available. These may include a donor lymphocyte infusion, chemotherapy, a second transplant, immunotherapy, or a clinical trial.

- Secondary cancer. A new, unrelated cancer may occur after successful treatment of the first cancer. Stem cell transplant recipients have a higher risk of developing secondary cancers. Therefore, lifelong cancer screenings are important for transplant patients.

For more information about survivorship and follow-up care, visit www.LLS.org/survivorshipworkbook to view the free LLS booklets *Navigating Life During and After a Blood Cancer Diagnosis* for adults, young adults and children.

Post-transplant care guidelines have been developed for patients (see *Other Transplant Organizations* on page 54) and doctors (see *References* on page 64). It is important for patients to discuss any symptoms they are experiencing with members of their healthcare team.

Clinical Trials for Blood Cancers

Every new cancer drug goes through a series of carefully controlled research studies before it can become part of standard cancer care. These research studies are called clinical trials and they are used to find better ways to care for and treat people with cancer.

In the United States, the FDA (Food and Drug Administration) requires that all new drugs and other treatments be tested in clinical trials before they can be used. At any given time, there are thousands of cancer clinical trials taking place. Doctors and researchers are always looking for new and better ways to treat cancer.

Researchers use cancer clinical trials to study new ways to:

- Treat cancer using:
  - A new drug
  - A drug approved to treat a different kind of cancer
  - A new combination of drugs
  - A new way of giving a drug (pill, intravenously [IV], etc.)
- Manage cancer symptoms and ease treatment side effects
- Find and diagnose cancer
- Keep cancer from coming back after treatment
- Manage long-term side effects

By taking part in a clinical trial, patients can see doctors who are experts in their disease, gain access to new, cutting-edge therapies, and provide helpful information for future patients. The treatments and information we have today are due in large part to patients being willing to join clinical trials. Anyone interested in being part of a clinical trial should talk to their hematologist-oncologist about whether a clinical trial might be right for them. During this conversation it may help to:

- Have a list of questions to ask about the risks and benefits of each trial (visit www.LLS.org/WhatToAsk for lists of suggested questions).
- Ask a family member or friend to go with you to your doctor visit—both for support and to take notes

Clinical trials can be difficult to navigate and figure out, but The Leukemia & Lymphoma Society is here to help. Patients and caregivers can work with **Clinical Trial Nurse Navigators** who will help find potential clinical trials, overcome the barriers to enrollment and provide support throughout the entire clinical trial process. Our Clinical Trial Nurse Navigators are registered nurses who are experts in pediatric and adult blood cancers and clinical trials. Your Clinical Trial Nurse Navigator will:

- Talk with you about your treatment goals
- Help you understand the clinical-trial process, including your rights as a patient
- Ask you for details about your diagnosis (like past treatments, treatment responses, and your cancer genetic profile), your current health, and your medical history, because these might impact whether you can take part in certain clinical trials
- Help you understand how your finances, insurance coverage, support network, and ability and willingness to travel might impact your choice of a clinical trial

- Guide you and help you in your efforts to find and enroll in a clinical trial, including connecting you with trial sites
- Help deal with any problems you might have as you enroll in a trial
- Support you throughout the clinical trial process

Please call an LLS Information Specialist at (800) 955-4572 or visit www.LLS.org/CTSC for more information about clinical trials and the Clinical Trial Support Center at LLS.

Also, visit www.LLS.org/booklets to view *Understanding Clinical Trials for Blood Cancers*.

Normal Blood and Bone Marrow

Blood. Blood is the liquid that flows through a person's arteries and veins. It carries oxygen and nutrients throughout the body. It also carries away waste products. Blood is composed of plasma and cells.

Plasma. Plasma is largely made up of water in which many chemicals are dissolved. These chemicals each have a special role. They include:

- Proteins
  - Albumin. This is the most common blood protein.
  - Blood-clotting proteins (coagulation factors). They are made by the liver.
  - Erythropoietin. It is made by the kidneys that stimulates red blood cell production.
  - Immunoglobulins. These are cells that fight infection
- Hormones, such as thyroid and cortisol
- Minerals, such as iron and magnesium
- Vitamins, such as folate and vitamin B_{12}
- Electrolytes, such as calcium, potassium and sodium.

Blood Cells. Blood cells are formed in the bone marrow, a spongy tissue where blood cells grow and develop. Blood cells start as stem cells. The process of stem cells maturing into blood cells is called "hematopoiesis." The blood cells are suspended in the plasma. See **Figure 5** on page 50. Once the blood cell is created, it will develop into one of the three types of blood cells. These are

- Red blood cells (the cells that carry oxygen); they
  - Make up a little less than half of the body's total blood volume
  - Are filled with hemoglobin, the protein that picks up oxygen from the

lungs and takes it around the body. It binds with carbon dioxide (CO_2) and removes it from the cells and then brings it back to the lungs. When a person exhales (breathes out), the CO_2 is removed from the lungs.

- Platelets (cells that help blood clot); they
  - Are small cells (one-tenth the size of red blood cells)
  - Help stop bleeding from an injury or cut
  - Stick to the torn surface of the vessel, clump together, and plug up the bleeding site. They form a clot, with the help of proteins, such as fibrin, and electrolytes, such as calcium.
- White blood cells (WBCs) are cells that fight infections. The several types of WBCs include
  - Neutrophils and monocytes: These are "phagocytes" (eating cells) that ingest and destroy bacteria and fungi. Unlike red cells and platelets, monocytes can leave the bloodstream and enter tissues to attack invading organisms and fight off infection.
  - Eosinophils and basophils: WBCs that respond to allergens or parasites.
  - Lymphocytes: WBCs found mostly in the lymph nodes, spleen and the lymphatic channels, they are a key part of the immune system. Some enter the bloodstream. There are three major types of lymphocytes. They are
    - T lymphocytes (T cells)
    - B lymphocytes (B cells)
    - Natural killer (NK cells)

In healthy people, stem cells in the bone marrow produce new blood cells continuously. When blood cells are fully developed, they enter the bloodstream as it passes through the marrow and then circulates throughout the body. In babies, 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 blood-forming marrow. In adults, marrow is only found in the spine (vertebrae), hip and shoulder bones, ribs, breastbone, and skull.

Hematopoietic stem cells are found in the marrow. These stem cells are important because they can be transplanted. Some stem cells enter the bloodstream and circulate; there are not enough of them to be counted in standard blood tests. Doctors know how to stimulate the growth of these cells in the marrow and have them migrate into the bloodstream. Then a special technique called "apheresis" is used to separate them from the circulating blood so they can be collected and stored. Stem cells from the placenta and the umbilical cord of a newborn infant can also be harvested and used for future transplantation.

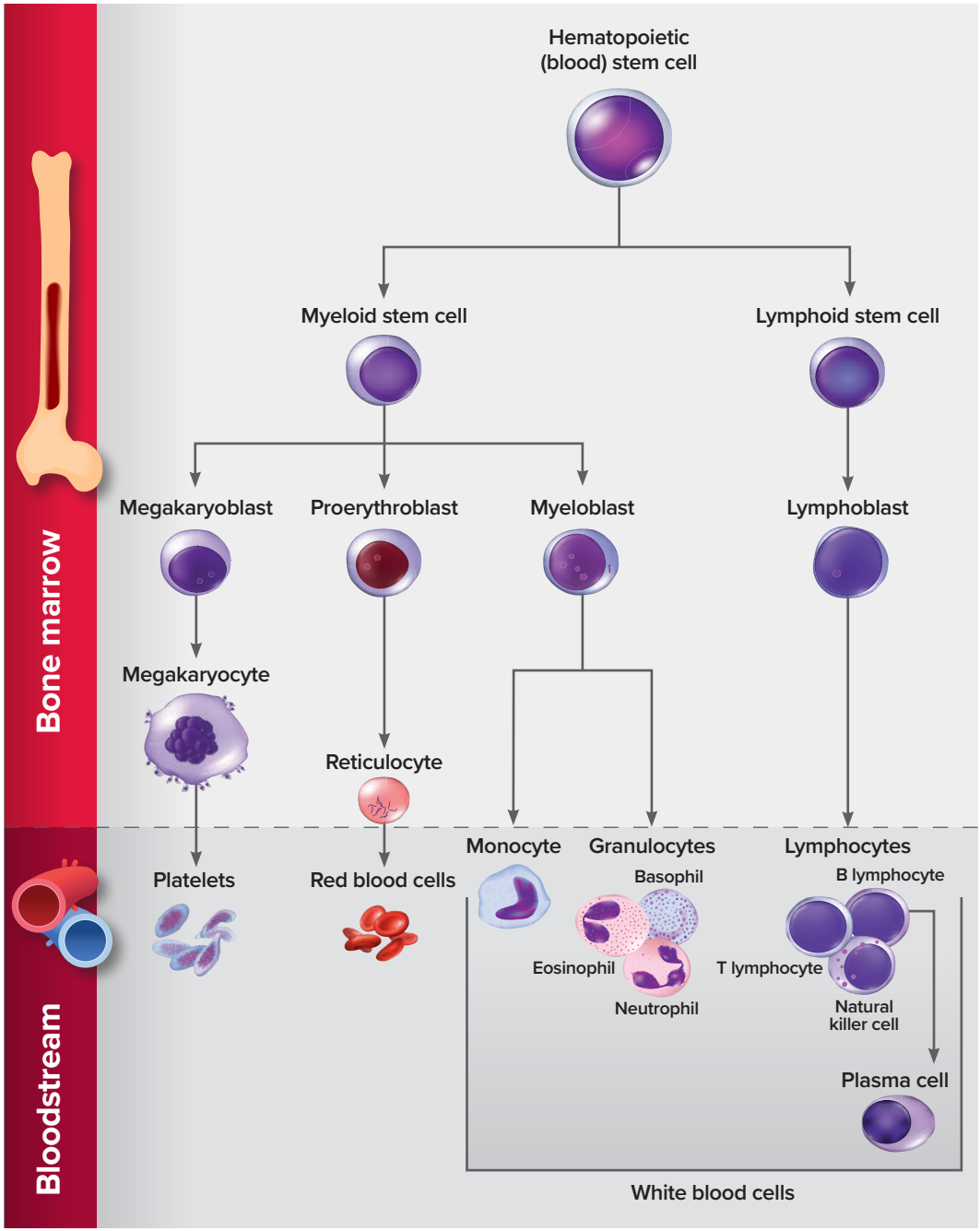

Figure 5. Most blood cells start as hematopoietic (blood) stem cells in the bone marrow. Hematopoietic stem cells are the most immature blood-forming cells. They must mature (go through many stages) to become a red blood cell, white blood cell or platelet. Some blood cells mature in the bone marrow. Other blood cells leave the bone marrow and travel to other parts of the body to develop into mature blood cells.

Resources and Information

LLS offers free information and services for patients and families affected by blood cancers. This section lists various resources you may find helpful.

For Help and Information

Consult with an Information Specialist. Information Specialists can assist you through cancer treatment, financial and social challenges and give accurate, up-to-date disease, treatment and support information. Our Information Specialists are highly trained oncology social workers and nurses. Language services are available. For more information, please:

- Call: (800) 955-4572 (Monday through Friday, 9 a.m. to 9 p.m. EST)
- Email and Live chat: www.LLS.org/InformationSpecialists

Clinical Trials (Research Studies). Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. Pediatric and adult patients and caregivers can work with our Clinical Trial Nurse Navigators who will help find clinical trials and provide personalized support throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.

Nutrition Consultations. Schedule a free one-on-one nutrition consultation with one of our registered dietitians who have expertise in oncology nutrition. Consultations are available to patients of all cancer types and their caregivers. Dietitians can assist with information about healthy eating strategies, side effect management and more. Please visit www.LLS.org/nutrition for more information.

Free Information Booklets. LLS offers free education and support booklets for patients, caregivers and healthcare professionals that can either be read online or ordered. Please visit www.LLS.org/booklets for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

Financial Assistance. LLS offers financial support to eligible individuals with blood cancer for insurance premiums, co-pays, and non-medical expenses like travel, food, utilities, housing, etc. For more information, please:

- Call: (877) 557-2672
- Visit: www.LLS.org/finances

Resources for Families. Blood cancer occurs in a small number of children. Families face new challenges, and the child, parents and siblings may all need support. LLS has many materials for families including a caregiver workbook, children's book series, an emotion flipbook, dry erase calendar, coloring books and a coloring app, a school reentry program, and other resources. For more information, please

- Call: (800) 955-4572
- Visit: www.LLS.org/FamilyWorkbook

Podcast. *The Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other healthcare professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Visit www.LLS.org/TheBloodline for more information and to subscribe to access exclusive content, submit ideas and topics, and connect with other listeners.

3D Models. LLS offers interactive 3D images to help visualize and better understand blood cell development, intrathecal therapy, leukemia, lymphoma, myeloma, MDS, MPNs and lab and imaging tests. Visit www.LLS.org/3D for more.

Free Mobile Apps.

- LLS Coloring For Kids™ – Allows children (and adults) to express their creativity and offers activities to help them learn about blood cancer and its treatment. Visit www.LLS.org/ColoringApp to download for free.
- LLS Health Manager™ – Helps you track side effects, medication, food and hydration, questions for your doctor, and more. Visit www.LLS.org/HealthManager to download for free.

Suggested Reading. LLS provides a list of selected books recommended for patients, caregivers, children and teens. Visit www.LLS.org/SuggestedReading to find out more.

Connecting with Patients, Caregivers and Community Resources

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Visit www.LLS.org/community to join.

Weekly Online Chats. Moderated online chats can provide support and

help cancer patients and caregivers reach out and share information. Please visit www.LLS.org/chat for more information.

Local Programs. LLS offers community support and services in the United States and Canada including the Patti Robinson Kaufmann First Connection® Program (a peer-to-peer support program), local support groups and other great resources. For more information about these programs or to contact your region, please:

- Call: (800) 955-4572
- Visit: www.LLS.org/LocalPrograms

Advocacy and Public Policy. Working closely with dedicated volunteer advocates, LLS's Office of Public Policy elevates the voices of patients to state and federal elected officials, the White House, governors and even courts. Together, we advocate for safe and effective treatments. We pursue policies that would make care more accessible to all patients. And, most of all, we advocate for the hope for a cure. Want to join our work? Visit www.LLS.org/advocacy for more information.

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, please visit www.LLS.org/ResourceDirectory to view the directory.

Additional Help for Specific Populations

Información en Español (LLS information in Spanish). Please visit www.LLS.org/espanol for more information.

Language Services. Let members of your healthcare team know if you need translation or interpreting services because English is not your native language, or if you need other assistance, such as a sign language interpreter. Often these services are free.

Information for Veterans. Veterans 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, please

- Call: the VA (800) 749-8387
- Visit: www.publichealth.va.gov/exposures/AgentOrange

Information for Firefighters. Firefighters are at an increased risk of developing cancer. There are steps that firefighters can take to reduce the risk. Please visit www.LLS.org/FireFighters for resources and information.

World Trade Center Health Program. People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get help from the World Trade Center (WTC) Health Program. People eligible for help include:

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area and those who lived, worked or were in school in that area
- Responders to the Pentagon and the Shanksville, PA, crashes

For more information, please

- Call: WTC Health Program at (888) 982-4748
- Visit: www.cdc.gov/wtc/faq.html

People Suffering from Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time, for example, if you feel depressed every day for a two-week period. For more information, please:

- Call: National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov and enter “depression” in the search box

Other Transplant Organizations

The American Society for Transplantation and Cellular Therapy (ASTCT)
(312) 321-6820
www.astct.org

The American Society for Transplantation and Cellular Therapy is an international professional association that promotes the advancement of blood and marrow transplantation and related cellular therapies both in clinical practice and in research.

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

Be The Match® helps patients who have leukemia, lymphoma and other

diseases and 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—and are also encouraged to contribute financially and/or volunteer. Patients and their families can also turn to Be The Match for support and resources before, during and after transplant. Post-transplant care guidelines have been developed for patients.

Blood & Marrow Transplant Information Network (BMT InfoNet)
(888) 597-7674
www.bmtinfonet.org

The Blood & Marrow Transplant Information Network (BMT InfoNet) provides transplant patients, survivors and their loved ones with emotional support and high quality, easy-to-understand information about bone marrow transplants, peripheral blood stem cell transplants and cord blood transplants.

The Bone Marrow & Cancer Foundation
(212) 838-3029 or (800) 365-1336
www.bonemarrow.org

The Bone Marrow & Cancer Foundation works to improve the quality of life for cancer and transplant patients and their families by providing vital financial assistance, comprehensive resources, educational information, physician referrals, and emotional support programs.

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

The Center for International Blood and Marrow Transplant Research leads a worldwide collaboration of scientists and clinicians to advance understanding and outcomes of hematopoietic stem cell transplantation. This research helps assess donor safety and helps identify the most promising transplant approaches and the patients most likely to benefit from a particular therapy.

DKMS
(212) 209-6700
www.dkms.org

The mission of DKMS is to fight against blood cancer and blood disorders by creating awareness, recruiting bone marrow donors, raising funds, improving therapies and supporting patients.

This international nonprofit provides information about registering to be a

donor, organizing donor drives, and the process of donating bone marrow.

DKMS is affiliated with the National Marrow Donor Program, so every person registered with DKMS is listed on the Be The Match Registry®.

Icla de Silva Foundation
(212) 593-1807
www.icla.org

The mission of the Icla de Silva Foundation is to save lives by recruiting bone marrow donors and by providing support services to children and adults with leukemia and other diseases treatable by marrow transplants.

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.

Health Terms

Allogeneic Stem Cell Transplantation. A treatment that uses donor stem cells to restore a patient's bone marrow and blood cells. First, the patient is given conditioning therapy (high-dose chemotherapy or high-dose chemotherapy with total body irradiation) 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 blood cells causing a decrease in 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.

Antigen. Any substance that causes the body to induce an immune response against that substance. Antigens include toxins, chemicals, bacteria, viruses, or other substances that come from outside the body.

Apheresis. The process of removing certain components of a donor's blood and separating out different parts of blood into plasma and distinct

types of cells including white blood cells, red blood cells, and platelets. The unneeded parts are returned to the donor. This procedure is also used to remove circulating blood stem cells, which can be frozen, stored and used later for transplantation instead of bone marrow stem cells.

Autologous Stem Cell Transplantation. A procedure in which stem cells are removed from a cancer patient, stored, and then given back to the patient after the patient undergoes intensive chemotherapy with or without radiation therapy.

Basophil. A type of white blood cell that fights against certain allergic reactions.

B Lymphocyte. A specialized white cell that produces antibodies in response to any foreign substance, and especially in response to bacteria, viruses and fungi. There are three types of lymphocytes, which are a vital part of the immune system and are important in the body's defense against infection. Also called "B cell."

Bone Marrow. The spongy tissue in the hollow central cavity of the bones, 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 because in these sites the marrow is filled with fat cells.

Central Venous Catheter (CVC). A tube inserted directly into a patient's vein (intravenously) that is used to take blood samples and administer therapies, medications, and other treatments. The thin tube is inserted and guided into a large vein, usually below the collarbone. A central venous catheter may stay in place for weeks or months to avoid the need for repeated needle-sticks. Also known as a "central line." The two most common types of central line are the (1) peripherally inserted central venous catheter (PICC or PIC Line) described above and the (2) implantable port. See: Port

Chemotherapy. The use of chemicals (drugs or medications) to stop the growth of cancer cells by either killing the cancer cells or by stopping them from dividing.

Comorbidity. The condition of having two or more diseases at the same time.

Conditioning Treatment. A process that usually includes chemotherapy either with or without radiation therapy that is used prior to autologous or allogeneic stem cell transplantation to prepare a patient's body for transplantation.

Cord Blood Stem Cells. Stem cells present in blood which is drained from a recent birthing mother's placenta and the umbilical cord to the baby. These stem cells can be infused into a patient's bloodstream to replace damaged or diseased stem cells.

Cryopreservation. A method of freezing and storing cells, tissues or organs to save them for future use.

Differentiation. The process by which immature cells become mature cells with specific functions. See Hematopoiesis.

Electrolytes. Minerals in the blood and other bodily fluids that carry an electric charge. Common electrolytes include calcium, chloride, magnesium, phosphorus, potassium and sodium. They can be acids, bases, or salts. The concentration of electrolytes in the bloodstream can be measured by different blood tests. Electrolytes affect body functions in many ways, including the amount of water in the body, the acidity of the blood (pH), muscle function and other important processes. The body loses electrolytes through sweating, and these must be replaced with electrolyte-containing fluid (generally by mouth [drinks] and sometimes intravenously [IV solutions]). Note that water does not contain electrolytes.

Engraftment. The process in which transplanted donor stem cells migrate to the recipient's bone marrow where they produce blood cells of all types.

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

Graft-Versus-Host Disease (GVHD). A condition caused when stem cells from a donor (the graft) attack the healthy tissue of the transplant patient (the host). The principal sites of injury to the patient are the skin, the liver and the gastrointestinal tract.

Graft-Versus-Tumor (GVT) Effect. An immune response in which transplanted donor's T lymphocytes (the graft) recognize and attack the malignant cells of the transplant recipient (the host). This response can occur only in allogeneic stem cell transplantation.

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

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.

Haploidentical Stem Cell Transplantation. A haploidentical transplant is a type of allogeneic stem cell transplantation that uses healthy, blood-forming cells from a half-matched donor to replace the unhealthy ones. The donor

is typically a family member. Parents are always half-match donors for their children, and siblings have a 50 percent chance of being a half-match donor for each other.

Hematologist. A doctor who specializes in the treatment of blood cell diseases. This doctor is a specialist who treats adults. A pediatric hematologist treats children.

Hematopathologist. A hematopathologist is a type of pathologist who studies diseases of blood cells by examining peripheral blood smears, bone marrow aspirates and biopsies, and lymph nodes and other tissues, and subsequently applies this expertise to identify diseases. A hematopathologist uses the information gathered from examining tissue samples under the microscope together with laboratory values, flow cytometry findings, and molecular diagnostic test results 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 on the diagnosis.

Hematopoiesis. The process of blood cell development in bone marrow. Undeveloped cells called stem cells develop into young or immature blood cells such as red blood cells or white blood cells of various types in a process called "differentiation." These young immature blood cells develop into fully functional blood cells during "maturation." The mature cells leave the marrow, enter the bloodstream, and circulate throughout the body. Hematopoiesis is a continuous process active throughout life. Most blood cells live for short periods and must be steadily replaced. Red blood cells die in 4 months, platelets die in 10 days, and most neutrophils die in 1 to 3 days. About 200 billion blood cells are made each day. When the bone 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.

Hematopoietic Stem Cell. See Stem Cells.

HLA(s). The abbreviation for "human leukocyte-associated antigen(s)." These antigens are proteins on the surface of most tissue cells that give individuals their unique tissue type. Human leukocyte-associated antigens play an important part in the body's immune response to foreign substances. HLA-associated antigen 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. HLA-associated antigen testing of a potential donor is done before a donor stem cell or organ transplant, to find out if there is a tissue match between the donor and the person receiving the transplant.

Host. The person (patient) who receives the donated living cells in a transplant.

Immune System. Comprises cells and proteins that defend the body against infection. Lymph nodes, lymphocytes, the spleen, and white blood cells are parts of the body's immune system.

Immunosuppressive Therapy. Medication that reduces the patient's natural immune system to prevent rejection of the graft (the newly implanted stem cells), and also helps prevent graft-versus-host-disease (GVHD).

Jaundice. A condition that occurs when the liver is not working properly. Signs of jaundice include yellowing of the whites of the eyes and darkening of urine.

Leukocyte. See White Blood Cell.

Lymph Nodes. Small structures, usually less than 1 centimeter, which contain large numbers of lymphocytes and are connected with each other by small channels called "lymphatics." These nodes are distributed throughout the body. See Lymphocyte.

Lymphocyte. A type of white blood cell that is essential in the body's immune system. There are three major types of lymphocytes: B lymphocytes, which produce antibodies to help combat infectious agents, such as bacteria, viruses and fungi; T lymphocytes, which have numerous 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.

Monocyte/Macrophage. A type of white blood cell that constitutes about 5 to 10 percent of the cells in normal human blood. Monocytes and neutrophils 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.

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

Neutrophil. The principal phagocyte (microbe-eating cell) in the blood. This white blood cell is the main cell that combats infection. Insufficient quantities of neutrophils in patients who have acute leukemia (and in patients after chemotherapy) increases their susceptibility to infection.

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

Oncologist. A doctor who diagnoses and treats patients who have cancer. An oncologist has special training to treat cancer in adults. Pediatric oncologists are specially trained to treat cancer in 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 infection 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 caused by bacteria, viruses, fungi, or protozoa to which individuals with a normal immune system are not usually susceptible, but patients undergoing transplant have weakened immune systems and infections are more likely to occur.

Pathologist. A doctor who identifies disease by studying tissues under a microscope.

Peripheral Blood. Blood that circulates throughout the body.

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 in a patient for weeks for administration of medications, fluids and nutrition. It can also be used for drawing 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 (one of the veins in the central venous system) that lies just above the heart. The PICC may eliminate the need for standard intravenous (IV) placement. After insertion, a portion of the PICC line remains outside the body. A nurse will connect a syringe to the external adapters of the PICC to administer medicines, parenteral nutrition or to draw blood samples for testing. PICCs must be flushed routinely and require regular dressing changes. See Port.

Phagocyte. A cell that 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 protective cells.

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

Platelets. Small fragments of blood cells (a platelet is about one-tenth the size of a red blood cell) that stick to the site of blood vessel injury, aggregate, and then seal off the injured blood vessel to stop the bleeding. Platelets are also called "thrombocytes," and disorders of platelets are called thrombocytopenia (too few platelets) or thrombocythemia (too many platelets).

Platelet Transfusion. A transfusion of donor platelets may be needed to support some patients who have been treated for blood cancer. The platelets can be collected from several unrelated donors and given as a pooled, random-donor unit. 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 a single donor by a procedure known as "apheresis." The platelets are skimmed from large volumes of blood passing through a specialized machine. The red blood cells and plasma are returned to the donor. The advantage of a transfusion that uses single-donor platelets is that the patient is not exposed to the spectrum of antigens on platelets from many different people. The recipient of this type of transfusion is less likely to develop antibodies against donor platelets. A related donor who has either an identical or very similar HLA tissue type can donate matched platelets for transfusion.

Port. A device used to draw blood and give treatments to patients who need medications on a regular basis. A port is a small two-part device with an implantable self-sealing part attached to a catheter (tube) to allow access to a vein. The port is implanted under the skin of the patient's chest. After the insertion site heals, no dressings are needed. To administer medicines, nutrition, or to draw blood samples for testing, 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. Another method for giving medicine on a regular basis is called Central Venous Catheter (CVC). See Central Venous Catheter.

Red Blood 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 blood cells make up about 40 to 45 percent of the volume of the blood in healthy individuals. Another term for red blood cell is "erythrocyte."

Reduced-Intensity Allogeneic Stem Cell Transplantation. A form of allogeneic transplantation in which 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-tumor effect). Sometimes called "nonmyeloablative stem cell transplantation."

Refractory Disease. Disease that is either resistant to or does not go into remission or improve substantially after initial therapy.

Regional Anesthesia. A temporary loss of feeling in a part of the body caused by special drugs called "anesthetics," which cause numbness in a particular area. The patient remains awake but has no sensation in the part of the body treated with the anesthetic. (Do not confuse this with "general anesthesia," in which the patient is rendered "unconscious" for a time and does not feel or recall anything.)

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 trace evidence of the disease remains. Long-term benefit usually requires a complete remission, especially in acute leukemia or progressive lymphoma.

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 and worn-out cells from the blood. The spleen is often affected in lymphocytic leukemia and lymphoma.

Stem Cells. Primitive cells that are essential to the formation of red blood cells, white blood cells and platelets. Stem cells are largely found in the bone marrow, but some leave the bone marrow and circulate in the blood. They are also found in the umbilical cord and placenta of newborn babies. Using special techniques, stem cells can be collected and used for stem cell therapy. See Hematopoiesis.

Systemic. Affecting the entire body.

T cell. A type of white blood cell. T cells are part of the immune system that help protect the body from infection and may also help fight cancer. Also called "T lymphocyte."

T-Cell Depletion. A process that decreases the number of T cells. Elimination of T cells from a bone marrow graft of a donor may reduce the chance of a patient incurring graft-versus-host disease.

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

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 cause clogging.

Umbilical Cord Blood. Blood from the umbilical cord of a newborn baby. This blood contains a high concentration of stem cells.

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

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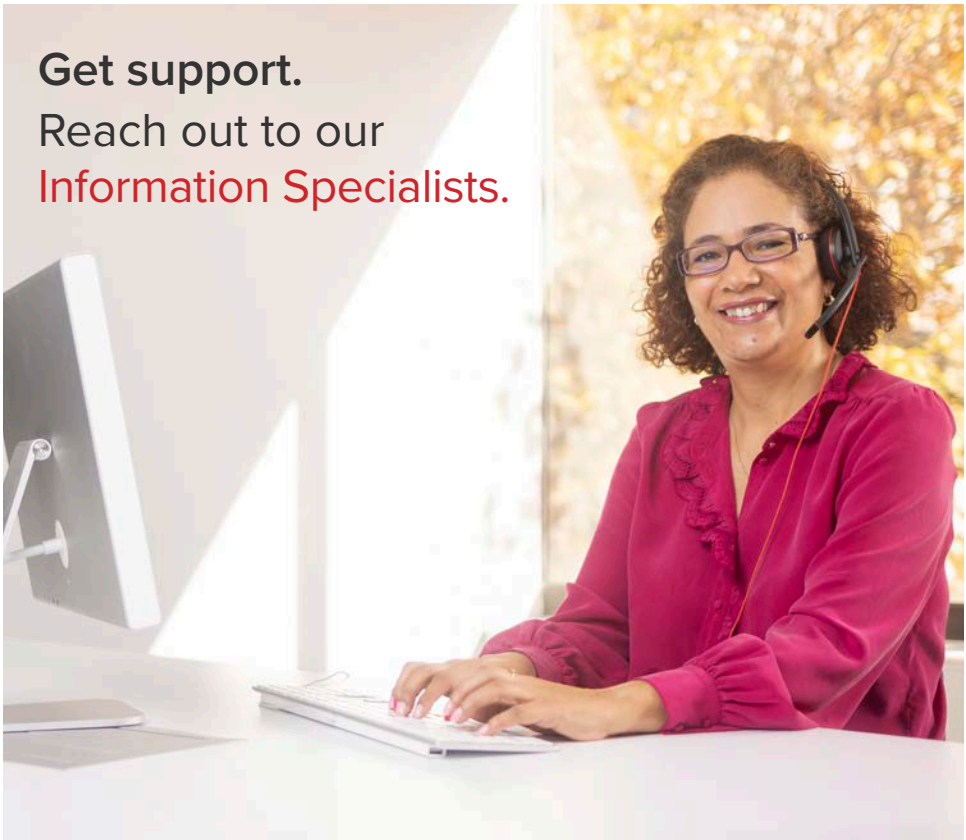

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