



**The Leukemia &
Lymphoma Society**[®]
Fighting Blood Cancers

Blood and Marrow Stem Cell Transplantation

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Table of Contents

Introduction	2
Overview of Stem Cell Transplantation	3
Normal Blood and Marrow	4
Origins and Basis of Transplantation	6
Disorders Treated with Stem Cell Transplantation	8
Immune Deficiency Diseases	8
Inherited Severe Blood Cell Diseases	8
Other Inherited Disorders	9
Aplastic Anemia	9
Leukemia, Lymphoma and Myeloma	9
Stem Cell Transplantation for Leukemia, Lymphoma and Myeloma	11
Testing to Identify Donors	13
Sources of Stem Cells	15
Marrow	15
Blood	16
Placental and Umbilical Cord Blood	17
T Lymphocyte Depletion	19
Stem Cell Selection Procedure	19
Types of Stem Cell Transplantation	20
Syngeneic Transplantation	20
Allogeneic Transplantation	20
Autologous Transplantation	22
Purging Autologous Marrow	22
Adverse Effects of Autologous Transplantation	23
The Transplant Procedure	23
Conditioning	23
Infusion of Stem Cells	24
The Immediate Post-Transplant Period	25
Special Issues – Allogeneic Transplantation	26
Side Effects of Conditioning Regimen	26
Infections	27
Graft Versus Host Disease	27
Nonmyeloablative Transplantation (Mini-Transplants)	30
Leaving the Hospital	32
Aftercare	33
Social and Emotional Aspects	34
Glossary	36
Resources	51

Introduction

This booklet provides information for patients and their families about blood or marrow stem cell transplantation for the treatment of leukemia, lymphoma or myeloma. Medical terms are defined in the glossary at the end of the booklet. We hope this information is of assistance. Comments about the information provided are welcome.

Between 1970 – when the transplant registry began tracking data – and today, the frequency of stem cell transplantation for the treatment of blood cancers has increased from hundreds to thousands of patients transplanted per year. An estimated 16,000 people in North America had autologous or allogeneic stem cell transplantation for blood cancers in 2003, the most current data available (Source: CIBMTR, Indications for Blood and Marrow Transplantation in North America in 2003.) The procedure continues to be improved in anticipation of making it a treatment option for even more patients each year. Before describing the technique and its applications further, a brief description of normal blood and marrow is provided for background.

This publication is designed to provide accurate and authoritative information in regard to the subject matter covered. It is distributed as a public service by The Leukemia & Lymphoma Society, with the understanding that The Leukemia & Lymphoma Society is not engaged in rendering medical or other professional services.

Overview of Stem Cell Transplantation

Stem cell transplantation is a technique that can restore the marrow function of patients who have had severe injury to that site. Marrow injury can occur because of primary marrow failure, destruction of marrow by disease, or intensive chemical or radiation exposure. The source for the earliest transplants was the marrow of a healthy donor who had the same tissue type (HLA type) as the patient. Usually, the source was a brother or sister. Donor programs have been established to identify an unrelated donor who has a tissue type that matches that of a patient. This approach requires screening tens of thousands of unrelated individuals of similar ethnicity to the patient.

The transplant is achieved by infusing a very small fraction of the marrow cells called “stem cells.” Stem cells not only reside in the marrow but a small number also circulate in the blood. They can be harvested from the blood by treating the donor with agents that cause a release of larger numbers of stem cells into the blood and collecting them by a process called hemapheresis. Stem cells also circulate in large numbers in fetal blood and can be recovered from placental and umbilical cord blood after childbirth. The harvesting, freezing, and storing of cord blood provide another source of stem cells for transplantation. Since blood and marrow are both good sources of stem cells for transplantation, the term “stem cell transplantation” has replaced “bone marrow transplantation” as the general term for this procedure.

If the donor and recipient are identical twins, the transplant is called “syngeneic,” the medical term for “genetically identical.” With a syngeneic transplant there is no immune difference and no likelihood of a host versus graft (graft rejection) or a graft versus host reaction. If the donor and recipient are not identical twins, the transplant is called “allogeneic.” An allogeneic transplant means the donor is the same species and, in practice, nearly always a match in tissue type to the recipient. The term “matched unrelated” is applied to the donor who is not a family member, recruited by searching among a large pool of potential donors for the rare individual who is identical or very similar in HLA type to the recipient.

The important technique of harvesting patients' stem cells in marrow or blood, freezing the collection and returning it to patients after they have received intensive chemotherapy and/or radiation therapy for their underlying disease is referred to as "autologous transplantation." This term is misleading since transplantation implies transferring tissue from one individual to another. This technique would better be referred to as "autologous stem cell infusion" (see *Autologous Stem Cell Infusion*).

Normal Blood and Marrow

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

- Proteins (such as albumin),
- Hormones (such as thyroid hormone),
- Minerals (such as iron),
- Vitamins (such as folic acid), and
- Antibodies, including those we develop from our vaccinations (such as poliovirus antibodies).

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

- The red cells make up half the volume of the blood. They are filled with hemoglobin, the protein that picks up oxygen in the lungs and delivers oxygen to the cells all around the body.
- The platelets are small cells (one-tenth the size of red cells) that help stop bleeding at the site of an injury in the body. For example, when an individual has a cut, the vessels that carry blood are torn open. Platelets stick to the torn surface of the vessel, clump together and plug up the bleeding site. Later, a firm clot forms. The vessel wall then heals at the site of the clot and returns to its normal state.
- The neutrophils and monocytes are white cells. They are called phagocytes (or eating cells) because they can ingest bacteria or fungi and kill them. Unlike the red cells and platelets, the white cells leave the blood and enter the tissues, where they can ingest invading bacteria or fungi and help combat infection. Eosinophils and basophils are two additional types of white cells that respond to allergens.

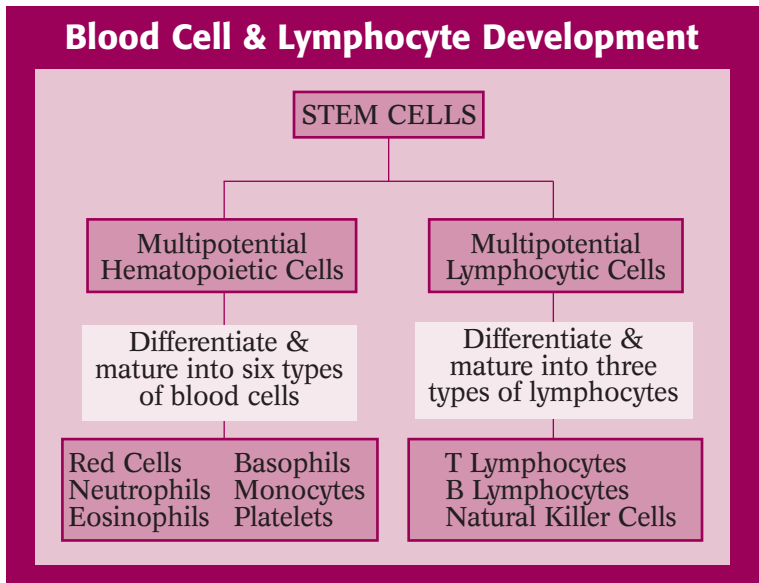


Figure 1. This figure depicts the process of stem cells developing into functional blood cells (hematopoiesis) and lymphatic cells in a simplified diagram.

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

Marrow is a spongy tissue where blood cell development takes place. It occupies the central cavity of bones. In newborns, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms, and legs no longer have functioning marrow. The backbones (vertebrae), hip and shoulder bones, ribs, breastbone, and skull contain marrow that makes blood cells in adults. Blood passes through the marrow and picks up formed red and white cells, and platelets, for circulation.

The process of blood cell formation is called hematopoiesis. A small group of cells, the stem cells, develop into all the blood cells in the marrow by the process of differentiation (see Figure 1).

When the fully developed and functional cells are formed, they leave the marrow and enter the blood. In healthy individuals there are enough stem cells to keep producing new blood cells continuously.

Some stem cells enter the blood and circulate. They are present in such small numbers that they cannot be counted or identified in the usual type of blood counts. Their presence in the blood is important because they can be collected by a special technique and can be transplanted into a recipient if enough stem cells are harvested from a compatible donor.

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

In summary, blood cells are made in the marrow. When the cells are formed and functional, they leave the marrow and enter the blood. The red cells and the platelets carry out their respective functions of delivering oxygen and plugging up injured blood vessels throughout the body. The white cells (neutrophils, eosinophils, basophils, monocytes and lymphocytes) enter the tissues (for example, the lungs) to combat infections, such as pneumonia, and perform other immune functions.

Origins and Basis of Transplantation

In the mid-19th century, Italian scientists proposed that the marrow was the source of blood cells. The idea that a factor in the blood-forming tissues from one individual might restore the injured marrow of another individual was considered a century ago. Some thought this factor was a chemical that could be transferred by eating the marrow. At the turn of the 20th century, scientists began to formulate the idea that a small number of cells in the marrow might be responsible for the development of all blood cells. They began to refer to them as “stem cells.” Attempts to use the marrow cells of a healthy individual to restore the lost marrow function of another person are more than 60 years old. Early attempts at human marrow transplantation were largely unsuccessful because the scientific basis for achieving successful outcomes was not yet known.

Marrow transplantation as a form of treatment began to be explored scientifically at the end of World War II. Stem cells are very sensitive to irradiation injury. Thus, marrow injury was an important and potentially lethal side effect of exposure to the atomic bomb or to industrial accidents in the atomic weapons industry. In the late 1940s, studies of marrow transplantation as a means of treating radiation-exposed combatants or civilians were spurred by the Atomic Energy Commission’s concern about the spread of nuclear technology and weapons.

The idea that medical disorders that affect blood cell or immune cell formation could be cured by marrow transplantation encouraged research by civilian scientists as well. These research efforts led to the current success of stem cell transplantation as a means of medical treatment and its increased availability to patients. Estimates from the Center for International Blood and Marrow Transplantation Research (CIBMTR) indicate that about 6,300 patients received allogeneic stem cell transplants for blood cancers in 2003 (the most current data.) CIBMTR estimates that about 9,300 patients received autologous stem cell infusions for blood cancers in 2003.

The basis for stem cell transplantation is that all blood cells and immune cells arise from stem cells in marrow.

A small number of stem cells also are in the blood. Drugs are available that increase the numbers of stem cells in the blood by drawing them out of the marrow. Sufficient quantities of stem cells for transplantation are obtained by circulating large volumes of blood through a hemapheresis machine and skimming off a sample that contains stem cells. Blood is an increasingly frequent source of stem cells for transplantation. Bone marrow transplantation (BMT), as a generic term for this procedure, has been modified to mean blood or marrow transplantation, permitting the continued use of the acronym, BMT. In many cases, the more specific term, stem cell transplantation (SCT) is used.

Disorders Treated with Stem Cell Transplantation

Immune Deficiency Diseases

Children who are born with severe immune cell deficiencies are unable to make lymphocytes, the cells that help the body combat infection. In the absence of normal lymphocytes and immune function, these children may experience repeated and often life-threatening infections. Lymphocytes (descendants of stem cells) can be restored by stem cell transplantation. Transplantation is actually aided by the recipient having a deficiency of immune cells; this makes it unlikely that the recipient will reject donor stem cells. Therefore, the recipient of transplantation for immune cell deficiency does not require intensive pretreatment (conditioning) with radiation or chemotherapy to suppress the immune system.

Inherited Severe Blood Cell Diseases

Marrow transplantation is used to treat inherited blood disorders, including thalassemia and sickle cell diseases. With these disorders, a mutant gene that is expressed only in the blood-forming cells is inherited. In this case, transplantation is a form of genetic therapy: the genetically abnormal blood-forming stem cells are replaced with normally functioning cells. A sibling with a matching tissue type is the stem cell donor. The dissimilarity of certain characteristics between two siblings is an advantage in this situation. The patient may have sickle cell disease (having received the mutant gene from both mother and father), and the sibling donor may be a carrier of the gene and have sickle cell trait (having received the mutant gene from mother or father, but not both), yet it is possible for stem cells from the donor to cure the recipient by replacing sickle cell disease, a very severe disorder, with sickle cell trait, a condition that does not cause any symptoms.

Major advances in stem cell transplantation techniques made it possible for the procedure to be useful in these situations. The high risk and serious side effects of transplantation delayed its use for these diseases, which, despite being very serious, are generally not immediately life-threatening. The decision regarding which patients with inherited blood cell disorders should take the risk of transplantation and when to undertake the procedure is still being studied.

Other Inherited Disorders

There is a group of inherited disorders in which there is a gene defect in the monocytes (a type of white cell). Soon after birth very disabling abnormalities including blindness, mental retardation, and severe neurological dysfunction may develop in the affected infant. Like all white cells, monocytes develop from stem cells. Abnormal monocytes can be replaced by normal cells through the transplantation of stem cells from a healthy compatible donor.

Aplastic Anemia

Stem cell transplantation has been used successfully to restore the function of marrow that has been injured. This type of marrow failure, referred to as aplastic anemia, can be drug induced, autoimmune, or, more rarely, inherited. As a result of exposure to certain drugs or to an external noxious agent, such as a chemical or unintended radiation exposure, marrow failure can occur. An autoimmune attack of the patient's lymphocytes on the blood-forming cells in the marrow can also cause failure. If the latter disease is severe, the marrow stops making blood cells. This alteration leads to the risk of serious hemorrhage from a deficiency of platelets or repeated and life-threatening infections from a deficiency of white cells. The marrow's blood cell manufacturing ability can be severely decreased also by the inherited disease called Fanconi aplastic anemia.

If severe, and if a compatible donor can be found, aplastic anemia can be treated by stem cell transplantation. In this situation, pretreatment of the patient with chemotherapy and/or radiation therapy is required to suppress the immune system of the patient and enhance the likelihood of success of the transplant.

Chemotherapy or radiation prior to transplant helps in these ways: it decreases the risk that the recipient's immune cells will reject the transplanted stem cells and it rids the recipient of the disordered lymphocytes that are often the cause of the condition (i.e., an attack by the patient's own lymphocytes on developing blood cells). The transplant cures the disease by providing the donor's lymphocytes and blood cells to replace those of the patient.

Leukemia, Lymphoma and Myeloma

Acute leukemia, lymphoma and myeloma have remission and cure rates that increase in relationship to the amount of chemotherapy given to the patient. Large doses of chemotherapy and/or radiation are required to destroy the disease cells. These intensive therapies can destroy normal cells in the marrow as well. The capability of the marrow to make healthy blood cells is so severely impaired after

very high-dose chemotherapy and/or radiation therapy required to treat refractory or relapsed disease that few patients would survive such treatment without replacement of the marrow. They would succumb as a result of infections (because of the absence of white cells) or hemorrhage (because of the absence of platelets).

Transplant physicians employ stem cell transplantation in order to be able to administer larger doses of chemotherapy or radiation therapy and restore normal blood cell production. Marrow function and blood cell production can be restored rapidly enough to allow recovery from the intensive treatment with the infusion of sufficient stem cells from a closely matched donor, such as a sibling. After several decades of research, discovery, and clinical trials, allogeneic stem cell transplantation can be used successfully to cure patients who are at high risk of relapse, who do not respond fully to treatment, or who relapse after prior successful treatment (see Table 1). Autologous stem cells (obtained from the blood and marrow of the patient) can be used in some circumstances.

Leukemia, lymphoma or myeloma that is poorly responsive to standard therapy, or has biological features that are known to predict for a poor response to chemotherapy, may be treated with very intensive chemotherapy and/or radiotherapy, which requires complementary allogeneic stem cell transplantation. The decision to use this treatment approach takes into account:

- The patient’s age, general health and medical condition
- The likelihood that the malignancy will respond to the conditioning regimen
- The availability of an HLA-matched donor

Table 1. Malignant Hematologic Diseases in Which Allogeneic Stem Cell Transplantation Has Been Used

Acute myelogenous leukemia (all subtypes)	Hodgkin lymphoma (if refractory to treatment or recurrent)
Adult acute lymphocytic leukemia	Idiopathic myelofibrosis (agnogenic myeloid metaplasia)
Childhood acute lymphocytic leukemia (if very high risk type or does not enter remission or relapses)	Lymphoma (all subtypes, if refractory to treatment or recurrent)
Chronic lymphocytic leukemia (all subtypes)	Myeloma
Chronic myelogenous leukemia	MDS (oligoblastic myelogenous leukemia)

Stem Cell Transplantation for Leukemia, Lymphoma and Myeloma

Two central questions should be answered when considering a transplant for a patient in remission:

- Does the current medical evidence indicate that stem cell transplantation will be more likely to cure the disease than other forms of therapy?
- Is there an appropriate donor available as a source of stem cells?

As stated in the previous section, other important factors that influence the decision include the patient's age, the specific disease being treated, biologic features at the time of diagnosis that indicate a poor prognosis, and the presence of complicating medical conditions (see Figure 2).

The age of the patient is a compelling factor in the decision to do a transplant. About three-quarters of individuals who develop leukemia, lymphoma or myeloma are over 50 years of age. Patients over that age are less likely than younger patients to have a favorable outcome after transplantation.

Indeed, the results of transplantation are best in children and become less favorable with each advancing decade. Older individuals are:

- 1) More susceptible to graft versus host disease,
- 2) More likely to have complicating medical problems, and
- 3) More likely to have a decreased tolerance for the accumulated effects of the prior intensive chemotherapy and the conditioning treatments required for transplantation.

These are generalizations, and allogeneic transplantation can be used in older individuals when judgment favors that decision. A modified form of allogeneic transplant, nonmyeloablative or mini-transplant, is being studied to determine its usefulness in older patients who are unlikely to be able to tolerate a standard allogeneic transplant. Nonmyeloablative stem cell transplant uses less conditioning chemotherapy and radiation therapy than standard allogeneic transplant.

Allogeneic Stem Cell Transplantation Decision Tree

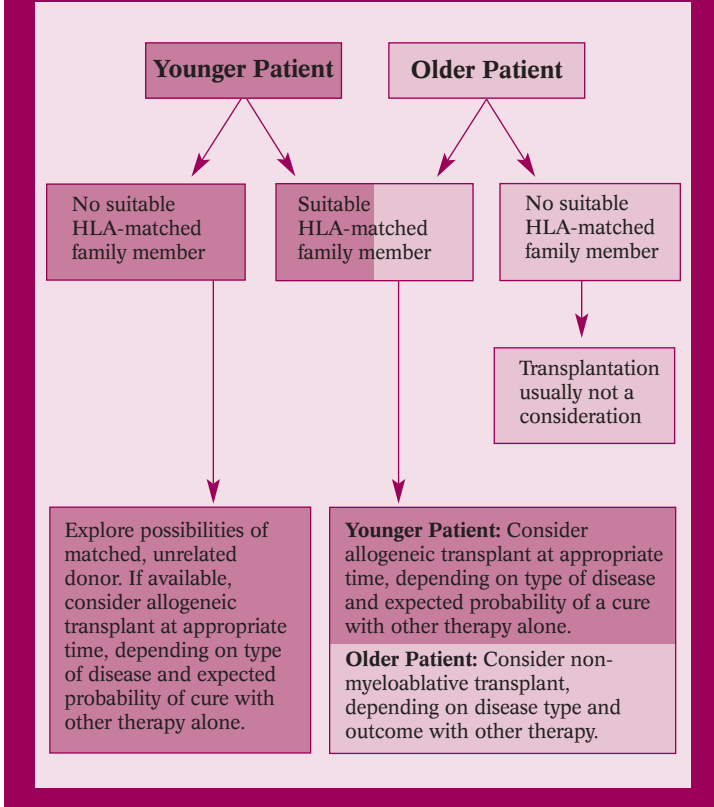


Figure 2. The option for SCT depends on the age of the patient, type of disease, expected treatment outcome without SCT and availability of a suitable HLA-matched family member.

See *Nonmyeloablative Transplantation* on page 30 for more information on this procedure. The risks of allogeneic transplantation have decreased with each succeeding decade of experience. Continued research may further improve the risk-versus-benefit in favor of transplantation. On the other side, new drugs and new therapeutic modalities may do the reverse.

Testing to Identify Donors

When a transplant is under consideration, the patient and his or her siblings will be tested to determine their tissue type or human leukocyte antigen (HLA) type.

The tissue type of an individual is determined by proteins on the surface of cells. Like other tissue cells, the leukocytes (white cells) contain these surface proteins. By testing the leukocytes obtained from a blood sample, transplant physicians can determine the HLA type of the patient and potential donors. The immune reactions that occur when nonidentical individuals receive a transplant are governed largely by these cell surface proteins. The lymphocytes of the recipient can sense that the donor's cells are "foreign" and attempt to kill (reject) them. The donor's immune cells can sense that the patient's cells are "foreign" and attack them.

The degree of difference in tissue type between donor and recipient is the main determinant of the intensity of:

- Host versus graft effect (the patient's cells reject the transplanted donor marrow or blood stem cells), or
- Graft versus host disease (the transplanted donor immune cells attack the patient's body).

These two reactions do not happen if the recipient and donor are identical twins. However, the fact that these reactions do happen in nonidentical siblings, even if they are matched by tissue typing, shows that HLA testing does not examine all relevant tissue type factors. In light of this fact, two processes are necessary to permit a successful transplant: suppression of the recipient's immune system before transplant and suppression of the donor's immune cells in the recipient after transplant.

A person's HLA type is governed by genes on chromosome 6 in tissue cells. All human somatic cell-types have 46 chromosomes: a pair of each chromosome numbered from 1 to 22 plus the two sex chromosomes (either XX in a female or XY in a male). The genes on the pair of chromosomes that determine HLA type are transmitted to a child as shown in Figure 3. One of each pair is inherited from one's mother (AB) and the other of the pair from one's father (CD). Each parent's contribution is referred to as a haplotype. The term haploidentical indicates that the potential donor who is being HLA-typed shares half the HLA type of the potential recipient. In the example shown in Figure 3, siblings AC and AD are haploidentical,

sharing their mother's chromosome A but each receiving different chromosomes from their father.

On average, a person has one chance in four of having the same HLA antigens as his or her sibling. Many patients will not have a sibling of the same tissue type.

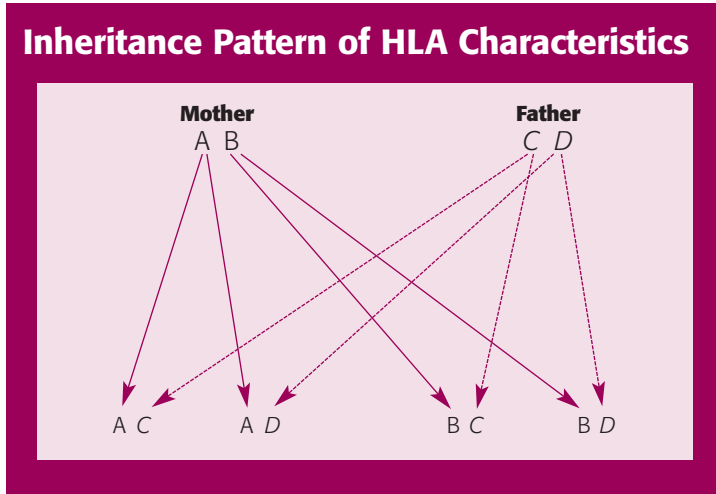


Figure 3. A and B depict the two chromosomes 6 of mother and C and D depict the two chromosomes 6 of father. The probability is that among four children, each will inherit the chromosome pairs shown, either A or B from mother and either C or D from father. Based on these outcomes, it is estimated that a match will occur on average one in four times. In other words, if child AC requires a transplant, a match should occur in one of four siblings on average. Of course, this probability holds true in large sample sizes; in an individual family, there might be no match or more than one match among siblings.

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

HLA types are determined by a method called molecular typing. In this technique, the DNA of the recipient and prospective donor are characterized to identify specific genes that direct the formation of the HLA antigens on the surface of cells.

Since the probability of finding a match among siblings is only one in four, efforts are being made to develop methods to permit transplantation between individuals who are only partially matched. For example, the ability to transplant from parent to child would make the availability of transplantation nearly universal for childhood disorders. Children's bodies are more tolerant of deviations from ideal matching, and hope exists that with better control of the immune reactions involved, moderately mismatched transplants may be feasible. Studies are underway to improve the delay in immune system recovery for recipients of partially matched (haploidentical) donor cells.

Sources of Stem Cells

Marrow

Obtaining marrow stem cells for transplantation requires that an appropriate donor receives a thorough health examination, which includes an electrocardiogram, chest x-ray, blood chemistry evaluation, and confirmation that blood cell counts are normal. The donor is tested to insure that hepatitis viruses and human immunodeficiency virus (HIV) are not present in the blood. The presence of a positive test for cytomegalovirus (CMV) does not necessarily prevent a person from being a donor.

Marrow donation is a surgical procedure. The donor is given anesthesia in an operating room suite. The transplant physicians use a special hollow needle attached to a large syringe to withdraw samples of marrow from the top edge of the pelvic bones. This area can be easily felt under the skin of the sides and back just below the waist. The insertion of the needle through the skin and into the rim of the pelvic bone is repeated until several pints of marrow are removed. The donor usually remains in the hospital for about 12 hours before going home. During this time, the donor recovers from both the anesthesia and the pain at the needle insertion sites. The donor can expect to feel some soreness in the lower back for a few days or longer. Most donors are back to their normal routine in a few days. Marrow is completely replaced within four to six weeks following donation.

The amount of marrow removed from the donor is related to the size of the recipient. A large adult requires more marrow cells than a small child does for the transplanted stem cells to engraft. The marrow is filtered to remove fragments of bone or tissue, passed through a screen to break up cell masses, and placed in a plastic bag from which it can be infused into the recipient's vein. The infusion of a suspension of cells containing the stem cells into the recipient's vein is similar to a blood transfusion. This type of administration is used whether the source of stem cells is marrow or blood.

The harvested marrow is usually administered to the recipient within a few hours and in most cases less than 24 hours. If necessary, the harvested marrow cells can be frozen and stored for later use. The marrow can be frozen for years and remain suitable for stem cell transplantation. For example, freezing is commonplace in anticipation of autologous marrow infusion (see *Autologous Transplantation* on page 22). In this circumstance, the patient's own stem cells are collected during a period of disease remission following treatment. The stem cells may be given back to the patient if a relapse occurs later and very intensive treatment is required.

Blood

The technique of human transplantation began with the supposition that the principal source of blood cell-forming stem cells is the marrow since this is the sole location for blood cell production after birth. It was known that stem cells leave the marrow, circulate in the blood, and re-enter the marrow. However, the scarcity of these cells in the blood made it seem an improbable source for transplantation.

Methods were developed to move stem cells from the marrow into the blood in sufficient numbers to be harvested and used for transplantation. The donor is treated with a drug that moves the stem cells into the blood. In some cases of autologous transplantation, stem cells can be mobilized by a combination of chemotherapy used to treat the underlying disease and stem cell-releasing cytokines. Then the cells are removed from the donor by a process called hemapheresis. In this process, the donor is linked to a special type of refrigerated centrifuge. The blood of the donor is pumped through the instrument, which separates the blood into four components: red cells, plasma, white cells and platelets. The latter two fractions are harvested because they contain the stem cells. The red cells and plasma are returned to the donor. Hemapheresis permits blood to be re-circulated through the machine for several hours. The procedure may be repeated at a later time, after which the collections are pooled. It generally takes two or more sessions to collect an adequate amount of stem cells from the bloodstream.

In this way, ample stem cells may be recovered to insure a successful transplant. The procedure avoids the general or spinal anesthesia required to harvest marrow stem cells from the donor and the few days of discomfort from the pelvic bone needle insertions required to recover marrow stem cells.

Placental and Umbilical Cord Blood

The placental and umbilical cord blood contains a significant number of blood-forming stem cells. At the time of delivery, the umbilical cord is severed and discarded as the “afterbirth” along with the attached placenta. Instead of being discarded, the blood from the placenta and cord can be carefully drained into a sterile plastic container. The suspension of cells containing stem cells can then be frozen and used for transplantation at a later date. When used as a transplant product, it is referred to as “cord blood stem cells.”

Collecting placental and umbilical cord blood is relatively simple. Immediately after a baby is delivered, the umbilical cord is clamped. The placenta and the remaining attached umbilical cord (the “afterbirth”) are then removed to an adjacent laboratory. The placenta is placed in a supporting frame. The surface of the cord is cleansed with povidone-iodine (Betadine®) and alcohol. Then a needle is inserted into the umbilical vein. The cord blood drains through the needle into a standard blood collection bag that contains an anticoagulant solution to keep the blood from clotting, to yield an average of 60 -120 milliliters. The white cells are separated from the red cells. An agent is added to the suspension of cells so they can be frozen without being damaged (a cryoprotective agent). The suspension, which includes stem cells, is then frozen for later use. Alternatively, the T lymphocytes present in the blood can be depleted or the stem cells enriched before freezing. (See *T Lymphocyte Depletion and Stem Cell Selection Procedure* on page 19.)

A second method involves collecting the cord blood after delivery of the baby, while the placenta is still in the mother’s womb. This method is theoretically advantageous for two reasons. First, the collection begins earlier, before the blood has a chance to clot. Second, it uses the contractions of the uterus in addition to gravity to enhance blood drainage. On the other hand, the technique is more intrusive and has the potential to interfere with after-delivery care for the mother and infant. This method may be preferred when collecting cord blood for a sibling who needs a transplant because there is less risk of losing the collection due to blood clotting or other reasons.

The cord blood collected from a single placenta is called a cord blood unit. The cord blood unit is transported to a facility for testing, freezing and long-term storage. Testing procedures include HLA-typing to determine the level of matching to potential recipients, cell counts and testing for infectious agents. Both commercial and non-profit facilities (cord blood banks) store and collect cord blood stem cells. Since there are millions of healthy births each year, even a small proportion of these afterbirth specimens can provide a potential source of stem cells for recipients who do not have a sibling with a similar tissue type.

Children and small-to-medium-sized adults usually can be treated from cord blood stem cell transplant. However, the number of stem cells from the cord and placenta may be insufficient to transplant large recipients successfully. Research studies are underway that are exploring ways to increase the number of stem cells in each cord blood unit and to combine two cord blood units to address the needs of adults and larger children.

There are other important considerations in using cord stem cells. Please see the Society's fact sheet, *Cord Blood Stem Cell Transplantation* for more information.

T Lymphocyte Depletion

T lymphocytes in a donor's marrow or blood cause graft versus host disease. In order to minimize this harmful reaction, the marrow or blood cell collection to be used for transplant can be treated with agents that can decrease the number of T lymphocytes infused with the stem cells. This technique reduces the incidence and severity of graft versus host disease. The procedure is known as "T lymphocyte depletion."

Transplant physicians must be careful about how many T cells are removed during this procedure because T lymphocytes are also beneficial. They help the donated stem cells take hold (engraft) and grow in the recipient's marrow. In some cases, T lymphocytes attack the leukemia cells, enhancing the results of other treatment. Known as graft versus leukemia, this effect can be seen mostly in myelogenous leukemia. The attack on the remaining blood cancer cells makes it less likely that the disease will return after transplant.

Stem Cell Selection Procedure

When an allogeneic donor's marrow or blood is collected, the stem cells are mixed with many other cells that are present in those sites. Lymphocytes are among the other cell types present. There are specific features on the outer coat of stem cells that permit them to be removed selectively from a mixture of cells and then recovered. When this selection procedure is done, it results in a cell population that is enriched in stem cells and has many fewer other cells, including lymphocytes. By reducing the number of T lymphocytes, the frequency or severity of the graft versus host immune reaction can be decreased.

Types of Stem Cell Transplantation

Syngeneic Transplantation

Syngeneic transplantation is the term used when the donor and recipient are identical twins, with identical genetic make-up and the same tissue type. With this type of transplant, donor cells are not rejected and the recipient's tissues are not attacked by the donor's immune cells (lymphocytes).

Allogeneic Transplantation

Allogeneic transplantation is the term for a transplant between two individuals. The term also implies that the donor's tissue type closely matches the recipient's. The donor who has the potential to match the prospective recipient most closely is the sibling of the patient, since both received their genetic composition from the same parents. Siblings do not always have closely matched tissue types, but the probability for a close match is much greater than among unrelated individuals.

Transplant physicians can test to determine the degree of compatibility before a decision is made to use the donor. Compatibility is assessed by laboratory tests that identify the tissue type of donor and recipient. There are two types of allogeneic donors:

- Related allogeneic donors, usually sibling donors
- Unrelated allogeneic donors, usually found within very large pools of volunteers, and matched to a tissue type that is the same as the patient's. Transplantation from a *matched unrelated donor* is sometimes referred to as "MUD" transplant.

Both related and unrelated allogeneic transplantation differs from either syngeneic or autologous transplantation in that the following may occur: _____

- The immune rejection of the donated stem cells by the recipient (host versus graft effect).
- The immune reaction by the donor's cells against the tissues of the recipient (graft versus host disease).

The immune rejection or host versus graft effect is usually prevented by intensive treatment of the recipient before the transplant (conditioning) to suppress the immune system. The immune reaction or graft versus host disease is combatted by

Autologous Transplantation for a Blood Cancer

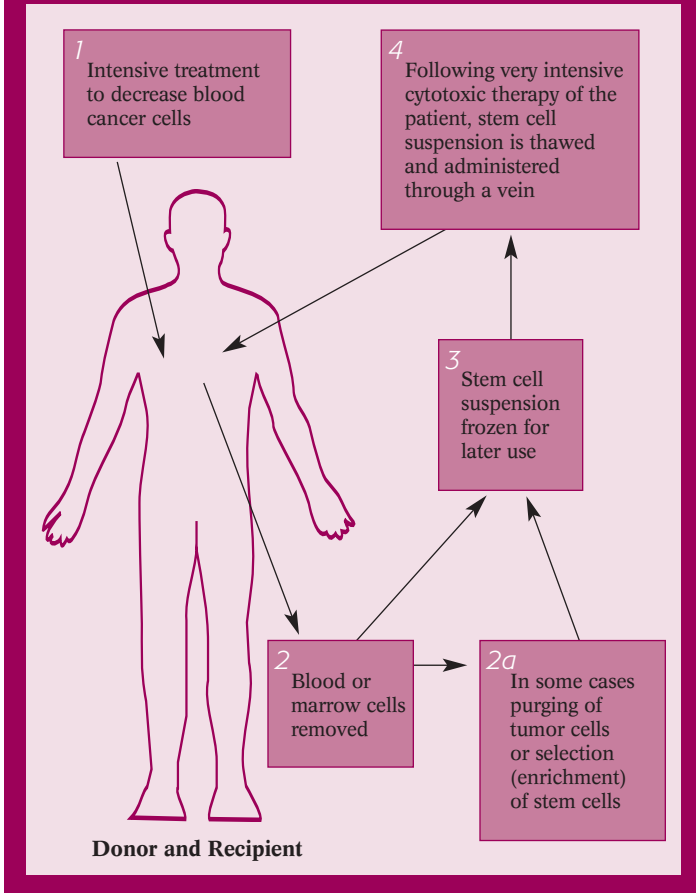


Figure 4. For autologous transplantation, stem cells are obtained from the patient who is treated intensively (1) to control the disease and to markedly decrease the cancer cells in marrow and blood. If the marrow is the source of stem cells, the patient is taken to the operating room, anesthetized, and the marrow is removed under sterile conditions. If blood is used as the source of stem cells, the patient is treated with granulocyte-colony stimulating factor (G-CSF), Neupogen® (filgrastim) alone or after chemotherapy, which draws stem cells out of the marrow and into the blood. The stem cells from blood or marrow are then harvested (2). In some cases, the marrow may be purged of cancer cells. Alternatively, stem cell selection can be used to deplete contaminating tumor cells (2a). The cells are treated with a cryoprotective agent so that they can be frozen and later thawed without injury (3). At a later time, when the patient is treated intensively again, the frozen stem cell suspension is thawed and infused into the patient so that blood cell production can be restored (4). The patient's marrow may contain small but significant numbers of residual malignant cells that are not apparent when a marrow sample is microscopically examined. "Purging" may selectively rid the marrow of these unwanted cells. Autologous blood or marrow transplantation does not carry the risk of either graft rejection or graft versus host disease and thus does not require conditioning treatment or immunosuppressive treatment. However, the patient does receive very intensive cytotoxic therapy to kill residual leukemia, lymphoma or myeloma cells. The autologous stem cells are used to restore blood cell production, thereby making chemotherapy and radiation therapy tolerable.

giving drugs to the recipient after the transplant to reduce the ability of the donated immune cells to attack and injure the patient's tissues (see *Graft Versus Host Disease* on page 27).

Autologous Transplantation

Autologous stem cell transplantation is an important therapy. Strictly speaking, it is not transplantation; it is a technique of obtaining stem cells from an individual's blood or marrow and infusing them back into the same individual. There are no immune-related transplantation issues with this procedure. Nonetheless, it is usually conducted in a transplant facility, supervised by transplant specialists, and is usually referred to as autologous blood or marrow stem cell transplantation. To be feasible, the procedure requires that an individual has sufficient numbers of healthy stem cells in marrow or blood despite the disease for which he or she is being treated. For example, in patients with acute leukemia, remission is usually achieved before the patient's marrow or blood is harvested and frozen for later use (see Figure 4).

The principal concerns in autologous transplantation are:

- First, that the amount of stem cells harvested is adequate to engraft when returned to the patient.
- Second, that tumor cells in the cell suspension used for transplant are removed or made incapable of re-establishing the tumor.

The use of autologous stem cells to restore blood cell production after intensive radiation and/or chemotherapy has been expanded to the treatment of pediatric and adult patients with a variety of cancers other than leukemia, lymphoma or myeloma.

Purging Autologous Marrow

When autologous marrow or blood stem cells are the source of the transplant, one concern is the possibility that the patient's cancer cells (e.g., leukemia, lymphoma or myeloma cells) will be reintroduced after intensive therapy. For example, if a patient in remission with acute myelogenous leukemia is to be given intensive pre-transplant conditioning and during the remission, transplanted with stem cells harvested from his or her own marrow, there is a risk of reintroducing some leukemia cells. To avoid this, the marrow may be treated to rid it of cancer cells after it is harvested and before it is frozen. Several techniques are being studied to determine the best method for purging cancer cells, including using antibodies specifically targeted to the cancer cells but harmless to the stem cells. However, the role of purging in the long-term success of autologous transplantation is still undetermined.

Adverse Effects of Autologous Transplantation

The main adverse effects of this procedure are the result of the high-dose chemotherapy and/or radiotherapy that is used to further destroy remaining cancer cells. Markedly decreased blood counts may lead to infection. Patients may need transfusions of red cells (for anemia) or platelets (to prevent or treat hemorrhage). Certain drugs can result in specific organ injury, such as lung complications, especially interstitial pneumonia, which may be the result of infection or damage from intensive therapy. Painful oral ulcers, called oral mucositis, may develop and can, in the extreme, prevent fluids or solids from being taken by mouth. Palifermin (Kepivance®), given by IV, can be used to prevent or minimize the effects of intensive therapy on the lining of the mouth. Graft versus host disease and graft rejection are not side effects since there is no donor/recipient incompatibility.

The Transplant Procedure

Conditioning

Blood cancer patients receiving an allogeneic transplant are treated initially with conditioning therapy. This treatment has two functions:

- 1) To make a recurrence of the cancer less likely by intensively treating the remaining cancer cells, and
- 2) To minimize the chance of stem cell graft rejection by inactivating the patient's immune system.

The conditioning therapies used are based on the disease being treated. Generally, two regimens are used for treatment, although programs vary among transplant centers:

- Either several drugs are given together, such as cyclophosphamide (Cytosan®), busulfan (Myleran®), cytarabine (Cytosar®), melphalan (Alkeran®), or etoposide (VePesid®, VP-16), or
- Chemotherapy is given along with total body irradiation.

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

Table 2. Side Effects of Conditioning Treatment

Nausea and vomiting	Occlusions of veins in liver
Diarrhea	Congestive heart failure
Ulcers in mouth	Premature menopause*
Hair loss	Sterility*
Loss of blood cell formation	Growth retardation*
Pneumonitis (pneumonia)	Cataracts*
Bleeding into urine from bladder	

** These effects are more likely to occur if total body irradiation is required for conditioning.*

Infusion of Stem Cells

The infusion process consists of the following:

- The donor stem cell suspension (derived from marrow or blood) is collected in a plastic blood transfusion bag.
- The cell suspension is infused through the patient's vein, similar to a blood transfusion. Special filters are used to remove bone fragments, fatty particles, and large clusters of cells from the cell suspension before it enters the bloodstream if stem cells from marrow are infused.
- The infusion usually requires several hours. Patients are checked frequently for signs of fever, chills, hives, a fall in blood pressure, or shortness of breath.
- Patients often experience no side effects from the infusion. Occasionally side effects occur, but these can be treated and the infusion completed. In patients receiving frozen-thawed stem cell suspensions, reactions may occur from the cryopreservative. Side effects may occur such as headache, nausea, flushing, shortness of breath and others. These usually can be managed and the infusion completed.

Allogeneic Transplantation for Leukemia, Lymphoma and Myeloma

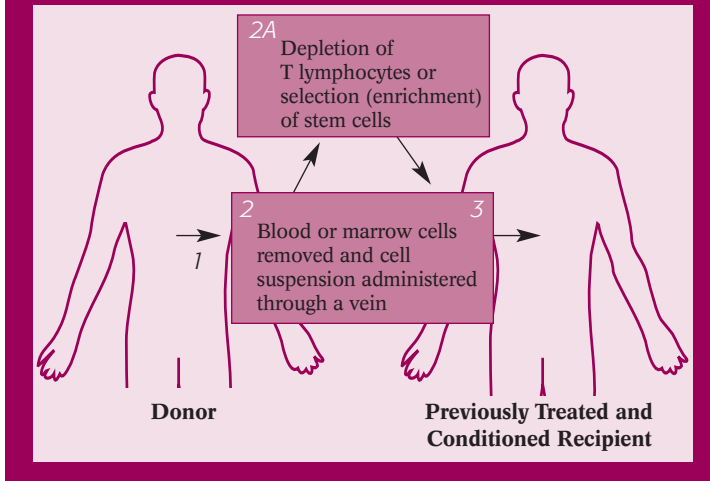


Figure 5. A histocompatible donor is identified, usually among the patient's siblings (see *Testing to Identify Donors* on page 13). The patient is anesthetized and marrow stem cells are harvested in an operating room. If blood is used as the source of stem cells, the donor is treated with granulocyte-colony stimulating factor [G-CSF, filgrastim (Neupogen®)], which draws stem cells out of the marrow and into the blood. The stem cells from blood are recovered by hemapheresis (1). The marrow cell suspension is filtered and placed in a plastic bag and the cell suspension is administered through a vein to the recipient, who has been treated intensively with total body irradiation and/or chemotherapy (2 and 3). In some cases, the stem cell suspension may be depleted of most T lymphocytes. Alternatively, stem cell selection may be employed, which also results in a marked decrease in T lymphocytes (2A), then the marrow is administered to the recipient.

The Immediate Post-Transplant Period

By the second or third day after the transplant, the effects of the intensive conditioning regimen and the decrease in marrow function begin to have their effects. The patient is kept in a protected environment to minimize contact with infectious agents (see *Infections* on page 27).

Two to five weeks after the transplant, the engraftment of donated cells becomes apparent by the appearance of normal white cells in the blood of the patient. Red cells and platelets are transfused periodically until marrow function is restored by the transplanted stem cells. The patient is monitored carefully by physical examinations, blood chemistries, imaging studies, and other tests to be sure major organs such as the heart, lung, kidneys, and liver are functioning normally. Periods of intravenous feeding, called hyperalimentation, may be needed in some patients to insure adequate nutritional intake in spite of poor appetite and diarrhea.

Special Issues - Allogeneic Transplantation

Most patients undergoing allogeneic transplantation for leukemia, lymphoma or myeloma require blood cell replacement, nutritional support, and special drugs to treat graft versus host disease.

Side Effects of Conditioning Regimen

The conditioning treatment prior to transplant can impair any system that is dependent on replacement by stem cells. In particular, the following areas of the body are very sensitive to cytotoxic drugs and radiation therapy:

- *Gastrointestinal tract:* Ulcers and dysfunction of the gastrointestinal tract frequently occur. Mouth sores (oral mucositis), nausea, diarrhea, intestinal cramps, and rectal or anal ulceration may be troublesome. A number of strategies, including the drug palifermin (Kepivance®), are used to minimize the severity of oral mucositis.
- *Skin:* Rashes may develop.
- *Hair follicles:* Hair loss is inevitable.
- *Lungs:* Particularly sensitive to the conditioning regimen, especially with total body irradiation following chemotherapy. A reaction called interstitial pneumonitis (pneumonia) can occur. This lung change is caused by a tissue reaction and does not mean that an infection is present. However, it can be very severe and prevent the efficient exchange of oxygen in the lungs.
- *Blood vessels:* Leaky blood vessels can be the result of the accumulated injury of chemotherapy and radiotherapy. Chemicals released from the immune reactions that occur after transplant also contribute to this effect by damaging vessel walls. Fluid escapes from the circulation and causes edema, or waterlogging of tissues. In the lungs, fluid accumulation can cause congestion, poor exchange of oxygen and shortness of breath.
- *Liver:* The blood vessels that lead into and pass through the liver are prone to blockage after transplantation. This serious side effect is called veno-occlusive disease (or VOD) because the veins are plugged. This effect results from toxic changes in the liver from chemotherapy and radiotherapy. The changes cause injury to the liver, which is reflected in jaundice (yellowing of the skin and eyes), and accumulation of fluid in the abdomen and elsewhere. Sometimes toxins normally removed by the liver can accumulate, leading to mental confusion and sleepiness.

Infections

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

When blood cell and immune cell levels are normal and when the skin and lining of the mouth and bowel are intact, the body easily fends off such microbes. These normal defenses are lost in transplant patients. For this reason, antibiotics and other antimicrobial drugs are sometimes administered to patients in anticipation of the development of infection. The drugs are usually continued until the white cells reappear in the blood in sufficient numbers to make infections unlikely. The term *opportunistic infection* applies to bacterial, fungal and viral agents that rarely cause infection unless severe immunodeficiency is present. A few such organisms are varieties of *Candida*, *Aspergillus*, *Pneumocystis*, or *Toxoplasma*.

Many precautions are taken to minimize the risk of infection. Measures to combat infection include the use of a single room with filtered air, limiting contact with visitors, use of masks, and meticulous hand washing by staff and visitors who enter the patient's room. Central line (indwelling catheter) sites must be kept clean. Patients are usually advised to eliminate uncooked fruits, vegetables, and other raw foods, which carry surface bacteria or fungi.

Unfortunately, several of these measures isolate the patient for the month or more that it takes for the donor stem cells to begin forming enough blood and immune cells to replenish the body's immune system.

Graft Versus Host Disease

Graft versus host disease (GVHD) is a condition in which the transplanted donor marrow or blood stem cells attack the patient's body (See Table 3).

This reaction occurs in many patients. It varies from barely perceptible to life-threatening and is most severe in older patients. With each advancing decade of age, the reaction occurs more frequently and severely. The severity of graft versus host disease depends on the differences in tissue type between patient and donor.

Table 3. Graft Versus Host Disease

Skin changes
•
Gastrointestinal tract malfunction
•
Liver injury
•
Other organ system impairment

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

GVHD may be acute or chronic. Acute GVHD can occur soon after the transplanted cells begin to appear in the recipient and, by definition, starts in the first 90 days after transplantation. The first signs are usually:

- A rash, with burning and redness of the skin that occur on the patient's palms or soles. The rash, along with the burning and redness, may spread to the patient's trunk and eventually develop over the entire body.
- Blistering can occur, and the exposed surface of the skin may flake off.
- Nausea, vomiting, abdominal cramps, and loss of appetite are signs of GVHD in the gastrointestinal tract. Diarrhea is common.
- Jaundice and pain in the abdomen indicate that GVHD has injured the liver, which also may be swollen.

Acute GVHD may be mild, moderate, or severe. It may be life-threatening if the manifestations are difficult to control.

Chronic GVHD usually occurs after the third month post-transplant and may not develop for a year or more after the transplant. As is the case with the acute reaction, older patients are more likely to develop chronic GVHD. It is more likely to occur in patients who previously have had acute GVHD.

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

The inside of the mouth and the esophagus (a tube that extends from the mouth to the stomach) may become excessively dry and damaged. Ulcers can result. The tendency to drying may lead to loss of tear formation and dryness of the vagina and other surfaces. The lungs also may suffer from the drying and scarring effects of the attack by the donor immune cells. Liver injury may result in failure of liver function and the flow of bile, which may not be overt but can be detected by blood chemical measurements. In severe cases, the bile may back up into the blood and cause jaundice. The chronic graft versus host reaction can be mild with later improvement, or more severe, persistent, and incapacitating.

Several drugs are used to prevent or minimize GVHD. The development of new drugs to treat GVHD, combined with early detection and advances in understanding the disease, have resulted in significant reductions in serious or fatal problems from GVHD. Successful treatments for both acute and chronic GVHD have been developed.

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

If acute GVHD does develop after transplantation, glucocorticoids such as methyl prednisone or prednisone in combination with cyclosporine are administered. New drugs and strategies that are available now or in clinical trials can supplement standard treatment. They include:

- Mycophenolate mofetil
- Alemtuzumab (Campath®) and other monoclonal antibodies
- Antithymocyte globulin (rabbit ATG)
- FK 506
- Sirolimus

Primary therapy for chronic GVHD is administration of steroids, usually cyclosporine and prednisone on alternating days. Clinical trials investigating steroid-refractory GVHD have reported some success for the following treatments:

- Tacrolimus
- Mycophenolate mofetil
- Thalidomide
- Daclizumab
- Extracorporeal photophoresis
- Infliximab
- Clofazimine

Drug dosages depend on the severity of the graft versus host reaction and whether the donor is related or unrelated.

Nonmyeloablative Transplantation (Mini-Transplants)

The preparation for an allogeneic stem cell transplant involves very high doses of chemotherapy drugs and/or radiation. Until recently, allogeneic stem cell transplant for patients ages 55 or older was relatively rare because the rigorous pre-transplant conditioning required is generally not well tolerated by these patients. For the same reasons, patients with poor overall health, especially those with poorly functioning internal organs, were also thought to be poor candidates for allogeneic stem cell transplant. Transplant physicians have been developing less strenuous pre-transplant conditioning regimens that may be suitable for a wider range of patients.

Although this new procedure is commonly called a mini-transplant, the term used by physicians is a “nonmyeloablative transplant.” This more accurate medical term is also very descriptive: “myelo” is a Greek word meaning “marrow” and “ablate” means “to destroy.” Thus, a nonmyeloablative transplant is one that does not completely destroy the patient’s diseased marrow. Patients being prepared for a nonmyeloablative transplant receive much lower doses of conditioning therapy.

The effectiveness of nonmyeloablative transplants depends on a reaction called graft versus malignancy (GVM), in which the recipient’s new immune system (originating from the donated stem cells) may destroy the bulk of remaining cancer cells. The procedure uses low rather than very high doses of either radiation or chemotherapy to condition the patient. Potent immune therapy is given to suppress the recipient’s T lymphocytes to avoid rejection of the donor stem cells. The goal is to have the

donor stem cells take up residence in the recipient's marrow and produce lymphocytes (immune cells) that attack the recipient's (patient's) blood cancer cells. If successful, the immune cells made from the donor's stem cells attack and suppress the residual leukemia or lymphoma cells in the recipient.

Nonmyeloablative transplantation may be advantageous for:

- Older patients and
- Patients with less rapidly progressive blood cancers.

Sufficient numbers of nonmyeloablative transplants have been performed to conclude that this may be an appropriate treatment for patients who are otherwise unsuitable for myeloablative stem cell transplant due to their advanced age or poor health. The GVM effect underlying the nonmyeloablative transplant procedure is strongest in patients being treated for chronic myelogenous leukemia (CML). Patients with other malignancies also benefit from GVM but to lesser degrees.

Because nonmyeloablative transplant is new, its risks and benefits have not yet been clearly established. However, one clear advantage is that a transplant may now be an appropriate option for individuals in their 60's and 70's. One disadvantage is that physicians have limited long-term survival data on nonmyeloablative transplant recipients. Survival rates for these patients cannot be compared with survival rates for those receiving fully myeloablative stem cell transplants or for those receiving chemotherapy or other non-transplant treatments until more data are available. Also, as is the case with allogeneic stem cell transplant, GVHD is an important and potentially disabling side effect of nonmyeloablative stem cell transplant.

Patients interested in exploring the possibilities of a nonmyeloablative transplant must locate a transplant center that is investigating the procedure through a clinical trial. (Clinical trials are experimental studies designed to test a new treatment's safety and effectiveness.) To locate transplant centers performing nonmyeloablative transplants, you can:

- Speak to your physician.
- Contact the Society's Information Resource Center at (800) 955-4572 or www.LLS.org.
- Contact the National Cancer Institute at 1-800-4-CANCER.
- Search on the Internet for the locations of clinical trials at the NCI's Web site: http://www.cancer.gov/clinical_trials.

Leaving the Hospital

Some transplant centers perform autologous transplantation on an outpatient basis. Some patients may have a portion of either an autologous or allogeneic transplant performed on an outpatient basis.

Most patients treated on an inpatient basis have recovered sufficiently to leave the hospital by three to five weeks post-transplant. Before discharge, both the physician and patient should feel comfortable that there are no remaining needs that require very close surveillance or hospital-based resources. There is variability among patients in the recovery of blood cell counts and the severity of other associated complications, especially graft versus host disease. Indications that patients are ready for discharge are:

- The patient's marrow is producing a sufficient number of healthy red cells, white cells and platelets.
- There are no severe treatment complications.
- The patient has a sense of well-being (as a result of restored blood cell counts). Mouth sores and diarrhea lessen or disappear.
- Appetite improves. It is important that patients are able to eat and drink to get sufficient fluid and nourishment before they are discharged from the hospital.
- The absence of fever and vomiting are also important.

Aftercare

In general, there is a shorter recovery period after autologous transplantation. The difficulties and restrictions described below mainly apply to allogeneic transplantation.

After discharge from the hospital, the patient continues to recover at home. Before leaving the hospital, patients and families are instructed in the continuing care needed at home. They learn what signs, such as fever, pain and diarrhea, should prompt a call to their healthcare provider. Home visits by nurses or physicians and patient visits to the outpatient clinic are important for follow-up and adjustment of activities and medications. Visits may be frequent at first. After several months, if all is going as anticipated, central lines (indwelling venous catheters) can be removed and the frequency of follow-up visits can be decreased.

It takes at least six to 12 months to recover nearly normal blood cell levels and immune cell function in a patient who receives an allogeneic transplant. During this time the following information applies:

- Patients should avoid contact with crowds, such as at shopping centers, religious services, parties and concerts, to reduce the risk of infection.
- Patients also may be advised to avoid contact with children who have had recent immunization with live viruses.
- The immunity that a patient may have had from previous vaccinations may be decreased, and re-immunization with vaccines made from inactivated organisms may be useful. If the patient was treated with total body radiation during conditioning, the lenses of the eyes would have become irradiated and there is the possibility that cataracts may develop.
- Irradiation of the gonads may lead to sterility in men and premature menopause in women. Hormone replacement is usually not necessary for men. For women, estrogen and progesterone replacement therapy may be needed.
- Children may have a slowed growth rate and may require growth hormone treatment and replacement of other hormones. In young patients, puberty may be delayed and hormonal therapy required.
- Radiation may decrease thyroid function and require that thyroid hormone be administered orally.
- The severity of chronic graft versus host disease is the major determinant of the patient's quality of life. This immune reaction can result in serious complications, including troublesome infections. Treatment for severe GVHD can also cause complications.

Social and Emotional Aspects

Individuals and families who consider a stem cell transplant for a blood cancer face not only physical but also certain emotional challenges. Patients and families face the risk of disease recurrence or progression and death if transplantation is not chosen or a possibility of an earlier death, severe side effects, or recurrence of the disease if transplantation is chosen. These challenges are counterbalanced by the hope of recovery and cure and the likelihood that new and better methods may make success more probable and the side effects less disabling.

The decision to undertake transplantation often is made under the intense pressure of severe illness, usually because of a medical crisis. There is a great deal of medical information to understand. Also, there are the mixed emotions created by whether or not a donor will be found and what is in store should one be found. If the transplant center is not nearby, the patient and family are placed under additional strains and are detached from support systems in their home community. The loss of autonomy, the isolation, the separation from work, school, friends, colleagues, and outside interests have to be endured.

There is disruption of family relationships as well. Children may worry about the outcome of a parent's illness and the separation from the father or mother. Parents suffer the uncertainty of the outcome of a child's treatment and the strain put on siblings and other family members and friends. The cost of the procedure and relocation of family, if necessary, is usually in the range of several hundred thousand dollars. Although much of this cost may be recovered from insurance, some will not.

The challenges of a long hospital stay, much of this in isolation; loss of well-being; and many potential, very uncomfortable, painful or disfiguring side effects add up to a difficult experience. Regardless of personal strength, the support of loved ones, nurses, physicians, and counselors is vitally important. Speaking with another person who has had a transplant can be helpful.

For most patients, the experience is psychologically challenging. However, many have a successful outcome and a return to vitality and to their school, job, or other roles and relationships.

There are programs to help ease the emotional and economic strain created by blood cancers. The Leukemia & Lymphoma Society offers patients financial assistance

and also provides the opportunity to join a support group or talk with a successfully treated patient with the same diagnosis.

To order publications or obtain information about The Leukemia & Lymphoma Society's programs and services for patients, call your local chapter or call the public Information Resource Center at (800) 955-4572.

You may also visit our Web site at www.LLS.org.

Glossary

Allogeneic Stem Cell Transplantation

The transfer of stem cells from one person to another who is not an identical twin. In the setting of allogeneic transplantation, an evaluation aims to find a donor who is very similar in tissue type to the recipient. The closer the similarity, the higher the probability that the transplant will be a success and harmful immune reactions will be minimized. Siblings of the same sex are the most likely to be closely matched, but other family members and unrelated matched donors can be similar enough to achieve a successful transplant if the optimal match is not available and the severity of illness justifies the risk.

Alloreactivity

The immune reaction between the immune cells of one individual and those of another individual. In stem cell transplantation, this immune reaction can occur in two directions because, unlike solid organ transplants, the donor “organ” contains many lymphocytes and later the donor stem cells will eventually make lymphocytes. The classic alloreactive direction is the host or recipient lymphocytes attacking the transplanted organ, so called “host versus graft disease” or more commonly called “graft rejection.” The other direction is graft versus host disease, in which the donor lymphocytes are mixed with the other cells infused and attack the recipient’s tissues (see Graft Versus Host Disease).

Anemia

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

Antibodies

Proteins that are made by B lymphocytes (especially their derivatives, plasma cells) in response to foreign substances called antigens. For example, infectious agents such as viruses or bacteria cause lymphocytes to make antibodies against them. In some cases (for example, the measles virus) the antibodies are protective and prevent a second infection (see Immune Globulins, Gamma Globulins). These antibodies can be used to identify specific cells and improve the classification of leukemia or lymphoma (see Immunophenotyping).

Antigen

A foreign substance that enters the body and stimulates the production of complementary antibodies by B lymphocytes. A foreign substance may stimulate the response of T lymphocytes as well. When bacteria infect a tissue, the immune system recognizes them as foreign and causes the B lymphocytes to create antibodies against them. These antibodies attach to the antigen. This attachment of antibodies to their antigen facilitates the ingestion of bacteria by bacteria-eating neutrophils (phagocytes). Transplanted cells can act to stimulate an immune response of a different type in which T lymphocytes of the recipient attack the cells perceived as foreign from the donor or T lymphocytes in the cell suspension from the donor can attack the tissue cells perceived as foreign in the recipient (see Graft Versus Host Disease).

Autologous Stem Cell Transplantation (Infusion)

This technique involves the harvesting of a patient's blood or marrow stem cells, which are often frozen for later use. The patient then is given intensive therapy, and the stem cells reinfused via an indwelling catheter. The blood or marrow stem cells may be obtained from a patient with a disease of the marrow when in remission (for example, acute myelogenous leukemia) or when the marrow is not overtly abnormal (for example, lymphoma requiring intensive therapy). Technically, this procedure is not transplantation, which implies taking tissue from one individual (donor) and giving it to another (recipient). The purpose of the procedure is to restore blood cell production from the preserved and reinfused stem cells after intensive therapy has severely damaged the patient's marrow. This procedure uses autologous blood stem cells with increasing frequency because marrow stem cells circulate in the blood and can be recovered there by hemapheresis (see Hemapheresis).

B Lymphocyte

One of three specialized lymphocyte types. They produce antibodies in response to any foreign substances, but to bacteria, viruses, and fungi in particular. These lymphocytes are a vital part of the immune system and are important to our defense against infection. The B lymphocytes mature into plasma cells, which are the principal antibody-producing cells.

Basophil

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

Bone Marrow

The bones are hollow and their central cavity is occupied by marrow, a spongy tissue that plays the major role in the development of blood cells. After puberty, marrow in the back bones, ribs, breast bone, pelvis, shoulders, and skull is most active in blood cell formation.

Cellular Immunity

That portion of the immune system that protects the individual from infection by the action of T lymphocytes. Deficiency in this portion of the immune system can permit infection by microbes such as the bacillus of tuberculosis, cytomegalovirus, and many others that might be fended off more easily in a healthy individual. T lymphocytes also cooperate with B lymphocytes to increase the effectiveness of antibody formation.

Central Line (see Indwelling Catheter)

Chemotherapy

The use of chemicals (drugs or medications) to kill malignant cells. Numerous drugs have been developed for this purpose. Most act to injure the DNA of cells. When the DNA is injured, the cells cannot grow or survive. Successful chemotherapy depends on the malignant cells being at least somewhat more sensitive to the drugs than normal cells. The cells of the marrow, the intestinal tract, the skin, and hair follicles are most sensitive to these drugs. Effects on these organs, such as mouth sores, diarrhea, rashes, and hair loss, are common side effects of chemotherapy.

Chromosome

All normal human cells with a nucleus contain 46 structures called chromosomes. The genes, specific stretches of DNA, are the principal structures that make up the chromosomes. An “average”-sized chromosome contains enough DNA to account for about 2,000 genes. The X and Y chromosomes are the determinants of our gender and are referred to as the sex chromosomes: two X chromosomes in females and an X and a Y chromosome in males. The number or shape of chromosomes may be altered in lymphoma or leukemia cells.

Clonal (monoclonal)

A population of cells derived from a single primitive cell. Virtually all neoplasms, benign and malignant (cancers), are derived from a single cell with an injury to DNA (mutated) and, thus, are clonal. The mutated cell has an alteration in its DNA, which forms an oncogene. This leads to its transformation into a cancer-causing cell. The

cancer is the total accumulation of cells that grow from the single mutated cell. Leukemia, lymphoma and myeloma are examples of cancers that are clonal, that is, derived from a single abnormal cell.

Colony Stimulating Factor (see Cytokines)

Conditioning Treatment

Intensive therapy with cytotoxic drugs or drugs and total body radiation before allogeneic stem cell transplantation. The therapy serves three purposes. First, it severely depresses the lymphocytes that are the key cells in the immune system. This action helps to prevent the rejection of the stem cell graft. Second, it markedly decreases the marrow cells. This may be important in order to open up the special niches that transplanted stem cells lodge in to engraft. Third, if the patient is being transplanted for a hematologic malignancy, this intensive therapy serves to greatly reduce any remaining tumor cells.

Cryopreservation

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

Cultures

If an infection is suspected, it is helpful to know both the principal site and the type of bacterium, fungus, or other microorganism involved so that the most specific antibiotic can be selected as treatment. To determine the site and organism, samples of body fluids such as sputum, blood, and urine and swabs of the inside of the nose, throat, and rectum are placed on culture medium in special sterile containers and incubated at body temperature (37° C, 98.6° F) for one to several days. These cultures are examined to see if bacteria, fungi, or sometimes other organisms are present in significant numbers. If they are present, the organisms can be tested with several antibiotics to learn which kills the organism. This is called determining the “antibiotic sensitivity” of the organism.

Cycle of Treatment

The term designates an intensive, clustered period of chemotherapy (and/or radiation therapy). This treatment, given for several days or weeks, represents one cycle of treatment. The treatment plan may call for two, three, or more cycles of the same or a slightly modified treatment. Cycles of treatment are the usual approach to the use of chemotherapy in the treatment of Hodgkin lymphoma or other lymphomas.

Cytokines

These are cell-derived chemicals that are secreted by various types of cells and act on other cells to stimulate or inhibit their function. Chemicals derived from lymphocytes are called “lymphokines,” and chemicals derived from lymphocytes that act on other white blood cells are called “interleukins,” because they interact between two types of leukocytes. Some cytokines can be made commercially and used in treatment.

Granulocyte-colony stimulating factor (G-CSF) or Neupogen® (filgrastim) is one such cytokine. It stimulates the production of neutrophils and shortens the period of low neutrophil counts in the blood of patients after chemotherapy. Cytokines that stimulate cell division are sometimes referred to as growth factors.

Engraftment

The process of transplanted stem cells homing to the recipient’s marrow and producing blood cells of all types. This occurrence is first evident when new white cells, red cells, and platelets begin to appear in the recipient’s blood following transplantation.

Eosinophil

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

Erythrocyte

A synonym for red cell (see Red Cell).

Fractionation of the Dose

In order to minimize the significant side effects of total body irradiation conditioning therapy, the dose of radiation required is given in several daily smaller doses rather than one larger dose. This approach has decreased the adverse effects of this treatment.

Gamma Globulins (see Immune Globulins)

Graft Versus Host Disease

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

Graft Versus Leukemia Effect

The immune reaction of transplanted T lymphocytes not only has the potential to attack the recipient's normal tissues (graft versus host) but to recognize and attack the malignant cells of the recipient. This effect was noted when: 1) leukemia recurrence after transplant was seen to be more likely if the donor and recipient were identical twins than if they were nonidentical siblings; 2) the more prominent the graft versus host disease the less likely was leukemia recurrence; and 3) the removal of donor T lymphocytes decreased graft versus host disease but also resulted in a higher frequency of leukemia relapse. Each of these observations could be explained best by an immune attack by donor lymphocytes against recipient leukemia cells that collaborated with the intensive conditioning treatment to keep the leukemia in check. This effect seems to be most active in myelogenous leukemia, although it may occur in patients with myeloma as well.

Granulocyte

A type of white cell that has a large number of prominent granules in the cell body. Other blood cells have fewer granules (e.g., lymphocytes). Neutrophils, eosinophils and basophils are types of granulocytes.

Granulocyte-colony Stimulating Factor (see Cytokines)

Growth Factors (see Cytokines)

HLA

The acronym for human leukocyte antigens. These proteins are on the surface of most tissue cells and give each individual his or her unique tissue type. Hence, the testing for HLA antigens is referred to as “tissue typing.” There are four major groups of HLA antigens: A, B, C, and D. These proteins act as antigens when donated (transplanted) to another individual, e.g., a bone marrow or stem cell recipient. If the antigens on the donor cells are identical (e.g., identical twins) or very similar (e.g., HLA-matched siblings), the transplant (donated marrow or cells) is more likely to survive in the recipient (engraft). In addition, the recipient’s body cells are less likely to be attacked by the donated cells (graft versus host disease).

Haplotype

The tissue type contributed by either the mother or father to his or her offspring. It is implied that it represents the genes on one parental chromosome. When a transplant procedure is between a donor and recipient that are haplotype identical, it means that the tissue type or HLA type of each is identical in respect to mother or father but not identical to the other. In some situations, if the discrepancy is not too great, the transplant may still be possible if the underlying disease makes the risk of partial compatibility warranted. Conditioning of the recipient and lymphocyte depletion of the donor stem cell suspension are steps taken to mitigate the risk of immune cell activation by the tissue type differences.

Hemapheresis

The process of removing a component of a donor’s blood and returning the unneeded components. The process uses continuous circulation of blood from a donor through an apparatus and then back to the donor. This process makes it possible to remove a desired element from large volumes of blood. Platelets, red cells, white cells or plasma can be removed selectively. For example, this technique permits the harvesting of enough platelets for transfusion from one donor (rather than six to eight separate donors). In so doing, the recipient of the platelets is exposed to fewer donors or can be given HLA-matched platelets from a single, related donor. This technique is also used to remove circulating blood stem cells, which can be frozen, stored, and later used for stem cell transplantation.

Hematologist

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

Hematopathologists are pathologists who specialize in the diagnosis of blood cell diseases and who perform the specialized laboratory tests often required to make a conclusive diagnosis.

Hematopoiesis

The process of blood cell development in the marrow. The most primitive cells in the marrow are stem cells. They start the process of blood cell development. The stem cells turn into young or immature blood cells, like red cells or white cells, of various types. This process is called “differentiation.” The young blood cells then further develop into fully functional blood cells. This process is called “maturation.” The cells then leave the marrow and enter the blood and circulate throughout the body.

Hematopoiesis is a continuous process that is active normally throughout life. The reason for this activity is that most blood cells live for short periods and must be continuously replaced. About five hundred billion blood cells are replaced each day. Red cells live about four months, platelets about 10 days, and most neutrophils for two or three days. This requirement for very rapid replacement explains the severe deficiency in blood cell counts when the marrow is injured by replacement with leukemia, lymphoma, or myeloma cells or by intensive cytotoxic treatment.

Host

The recipient of the transplant who acts as “host” to the transplanted stem cells.

Humoral Immunity

The portion of the immune system that produces antibodies. This portion of the system is represented by the various types of B lymphocytes that make antibodies and are scattered throughout the lymph nodes, other lymphatic tissue, and the bone marrow. B lymphocytes mature into plasma cells that produce antibodies.

Iliac Crest

The edge of the hip bone from which marrow is usually sampled for diagnosis of blood cell diseases.

Immune Globulins or Immunoglobulins

Proteins in the blood plasma which function as antibodies and play an important part in controlling infections.

Immunophenotyping

A method that uses the reaction of antibodies with cell antigens to determine the specific types of cells in a sample of blood cells, marrow cells or lymph node cells. A tag is attached to antibodies that react with specific antigens in the cells. The tag can be identified by the laboratory equipment used for the test. As cells carrying their array of antigens are tagged with specific antibodies, they can be identified; for example, myelogenous leukemia cells can be distinguished from lymphocytic leukemia cells. This method helps to subclassify cell types that may, in turn, help to decide on the best treatment to apply in that type of blood cancer.

Immunosuppression

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

Indwelling Catheter

Several types of catheters (e.g., Hickman[®], Broviac[®] and others) are used in patients receiving intensive chemotherapy and/or nutritional support. An indwelling catheter, also called a central line, is a special tubing inserted into a large vein in the upper chest. The catheter is tunneled under the skin of the chest to keep it firmly in place. The exposed end of the catheter can be used to inject medications, fluids, or blood products or to withdraw blood samples. With meticulous care, catheters can remain in place for very long periods of time (many months), if necessary.

Interleukin (see Cytokines)

Interstitial Pneumonitis

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

Intrathecal

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

Karyotype

The systematic arrangement, using photographs, of the 46 human chromosomes of a cell in 23 matched pairs (maternal and paternal member of each pair) by length from longest to shortest and other features. The sex chromosomes are shown as a separate pair (either XX or XY).

Leukocyte

A synonym for white cell (see White Cell).

Leukopenia

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

Lymph Nodes

Small structures, the size of beans, which contain large numbers of lymphocytes and are connected with each other by small channels called lymphatics. These nodes are distributed throughout the body. In patients with lymphoma, Hodgkin lymphoma, and some types of lymphocytic leukemia, the malignant lymphocytes grow and expand the lymph nodes so that they may be enlarged. This enlargement of lymph nodes can be seen, felt, or measured by computed tomography (CT) scan or magnetic resonance (MR) imaging, depending on the degree of enlargement and location.

Lymphocyte

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

Lymphokine (see Cytokines)

Mini-Transplant (see Nonmyeloablative Allogeneic Stem Cell Transplant)

Monoclonal Antibodies

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

Monocyte (macrophage)

A type of white cell that assists in fighting infection. The monocyte and the neutrophil are the two major microbe-eating and 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 and can combat infection in the tissues or can serve other functions, such as ingesting dead cells (scavenging).

Mucous Membranes

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

Neutropenia

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

Neutrophil

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

Nonmyeloablative Allogeneic Stem Cell Transplant

Also referred to as mini-transplants, a type of stem cell transplant that uses less induction chemotherapy and radiation. The theory being tested with a mini-allogeneic transplant is that by undergoing less-toxic methods prior to the transplant, the body is better able to withstand the transplant.

Oncogene

A mutated gene that is the cause of a cancer. Several subtypes of acute myelogenous leukemia, acute lymphocytic leukemia, lymphoma, and nearly all cases of chronic myelogenous leukemia have a consistent mutated gene (oncogene).

Oncologist

A physician who diagnoses and treats patients with cancer. This person is usually an internist, who treats adults, or a pediatrician, who treats children. Radiation oncologists specialize in the use of radiation to treat cancer, and surgical oncologists specialize in the use of surgical procedures to treat cancer. These physicians cooperate and collaborate to provide the best treatment plan (surgery, radiation therapy or chemotherapy) for patients.

Opportunistic Infection

A bacterial, viral, fungal or protozoan infection that usually does not cause disease in a healthy individual but can produce serious infections in persons with immune deficiency, such as those undergoing allogeneic stem cell transplantation.

Pancytopenia

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

Petechiae

Pinhead-sized sites of bleeding in the skin. This type of bleeding results from a very low platelet count. The small punctate hemorrhages are frequently seen on the legs, feet, trunk and arms. They disappear gradually when the platelet count increases.

Phagocytes

Cells that readily eat (ingest) microorganisms such as bacteria or fungi and can kill them as a means of protecting the body against infection. The two principal phagocytes in the blood are neutrophils and monocytes. A decrease in these blood cells is the principal cause of susceptibility to infection in patients with leukemia or those treated with intensive radiation therapy and/or chemotherapy, which suppresses blood cell production in the bone marrow.

Platelet Transfusion

The transfusion of donor platelets is frequently needed to support patients treated for leukemia or lymphoma. The platelets can be pooled from several unrelated donors and given as “pooled random-donor platelets.” Platelets from about six one-unit

blood donors are needed to significantly raise the platelet count in a recipient. Sufficient platelets can be obtained from one donor if his or her platelets are obtained by hemapheresis. The advantage of single-donor platelets is that the patient is not exposed to the different antigens on platelets from many different people and is less likely to develop antibodies against donor platelets. HLA-matched platelet transfusion can be given from a related donor with an identical or very similar HLA tissue type.

Platelets

Small blood fragments (about one-tenth the volume of red cells) that stick to the site of a blood vessel injury, aggregate with each other, and seal off the injured blood vessel to stop bleeding.

Polymerase Chain Reaction (PCR)

A technique to expand trace amounts of DNA or RNA so that the specific type of the DNA or RNA can be determined. This technique has become useful in detecting a very low concentration of residual leukemia or lymphoma cells, too few to be seen using a microscope. The technique can detect the presence of one leukemia cell among five hundred thousand to one million nonleukemic cells. PCR requires a specific DNA abnormality or marker, such as an oncogene, in the leukemia or lymphoma cells for its use.

Purging

The process by which tumor cells are removed from the marrow or blood cell suspension that is to be used for an autologous transplant. The stem cells used in an autologous transplant are obtained from the patient with leukemia, lymphoma or myeloma. An attempt is made to treat the patient and induce a remission before the stem cells are harvested, but some inapparent tumor cells are probably always present. Purging is used to try to further minimize returning tumor cells to the patient with the stem cells after intensive, and hopefully curative, cytotoxic treatment is given.

Red Cell

A blood cell that carries hemoglobin, which binds oxygen and carries it to the tissues of the body. The red cells make up about 45 percent of the volume of the blood in healthy individuals.

Relapse or Recurrence

A return of the disease after it has been in remission following treatment.

Remission

The complete disappearance of a disease, usually as a result of treatment. The terms “complete” or “partial” are used to modify the term “remission.” Complete remission means all evidence of the disease is gone. Partial remission means the disease is markedly improved by treatment, but residual evidence of the disease is present.

Resistance to Treatment

The ability of cells to live and divide despite their exposure to a drug that ordinarily kills cells or inhibits their growth. This is the cause of refractory malignant disease, whereby a proportion of malignant cells resist the damaging effects of a drug or drugs. Cells have several ways to develop drug resistance.

Spleen

An organ of the body that is in the left upper portion of the abdomen just under the left side of the diaphragm. It contains clusters of lymphocytes as lymph nodes do and also filters out old or worn-out blood cells. It is often affected in leukemia, especially the lymphocytic leukemias, lymphoma, and Hodgkin lymphoma. Enlargement of the spleen is referred to as splenomegaly. Removal of the spleen by surgery is referred to as splenectomy. Removal of the spleen can be done since most of its functions can be performed by other organs, such as the lymph nodes and liver.

Stem Cells

These are primitive cells in marrow that are important in making red cells, white cells and platelets (see Hematopoiesis). The stem cells are largely found in the marrow, but some leave the marrow and circulate in the blood. Using special techniques, the stem cells in blood can be collected, preserved by freezing, and later thawed and used for therapy.

T Lymphocyte Depletion

A process to decrease the number of immune cells that cause graft versus host disease. Typically antibodies against T lymphocytes are used to draw them out of the stem cell sample to be used for transplant. The decreased presence of T lymphocytes in the transplant minimizes the intensity of graft versus host disease. Since T lymphocytes help stem cells engraft and can suppress residual tumor cells in the recipient, some T cells are useful in the transplanted cells.

Thrombocytopenia

A decrease below normal in the number of blood platelets.

Tolerance

A very important event in the long-term success of transplantation. After a time, usually a year or so, the prior host and donor T lymphocytes die off and new lymphocytes are formed from the donor's engrafted stem cells. These "adapt" to the new host and stop attacking the recipient's cells. If tolerance is present, the immune system is no longer distracted and can serve the patient by working efficiently to protect against microbes. Risk of infection returns toward that of a healthy person. Immunosuppressive therapy can be stopped.

White Cell

A synonym for leukocyte. There are five major types of white cells: neutrophils, eosinophils, basophils, monocytes and lymphocytes.

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