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# CHAPTER 2

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## Basic Concepts of Transplantation

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### History of Transplantation

The area of hematopoietic stem cell transplantation (HSCT) has grown immensely since its beginnings. The roots of bone marrow transplantation (BMT) can be traced back to 1949 when Leon Jacobson and his colleagues performed mouse experiments and discovered that mice could recover from lethal irradiation if their spleens were shielded (Appelbaum, 1996). Lorenz, Uphoff, Reid, and Shelton demonstrated in 1951 that radiation protection could be provided with the infusion of syngeneic marrow. In 1955, Main and Prehn showed that mice protected with an allogeneic marrow infusion could permanently accept a skin graft from a marrow donor. By the mid-1950s, several laboratories had shown by cytogenetic markers that the radioprotective effect of BMT was the result of the replacement of the host's damaged hematopoietic system with healthy cells from a donor (Appelbaum, 1996). In 1959, Dr. E. Donnall Thomas initiated the first attempt to treat leukemia using high-dose chemotherapy followed by syngeneic (identical twin) marrow transplantation (Appelbaum, 1996). In early trials, transplantation using donors other than identical twins proved unsuccessful because of a lack of understanding of human leukocyte antigens (HLAs) and their importance to histocompatibility (Thomas, 1995). By the mid-1960s, it had been discovered, in dogs, that successful allogeneic marrow transplantation could be achieved by matching at the major histocompatibility complex (Appelbaum, 1996).

Many of the early transplants were unsuccessful because of only transient engraftment of cells and disease progression. The first successful allogeneic transplant for leukemia occurred in the late 1960s at the University of Minnesota. The donor was a matched sibling, and the recipient was an infant with an immune-deficiency disease (Appelbaum, 1996). The first unrelated allogeneic transplant was performed in 1973. Autologous marrow transplantation was first used successfully in patients with lymphoma in the late 1970s and became more widespread throughout the 1980s

(Appelbaum, 1996). Currently, HSCT is used in a wide variety of malignant, nonmalignant, and genetically determined diseases and is the only known cure for many malignant and nonmalignant diseases (see Table 2-1). Transplantation may be referred to by a number of different terms, including BMT, HSCT, peripheral blood stem cell transplant (PBSCT), or umbilical cord transplant.

HSCT is the transplantation of hematopoietic progenitor cells, which have the ability to proliferate, repopulate the marrow spaces, and mature. Blood counts and immunity are reestablished and recover when the mature blood cells enter the bloodstream (AABB et al., 2009). Historically, hematopoietic stem cells were collected from the bone marrow. Now physicians can select from three sources: bone marrow, peripheral blood, and umbilical cord blood (UCB) (AABB et al., 2009). The first successful PBSCTs were performed in the 1980s (Duncombe, 1997). This cell source is now used more often than bone marrow in adults undergoing allogeneic transplantation (Harris, 2010). Transplantation of UCB was successfully performed for the first time in 1988 to treat a child with Fanconi anemia. The patient received UCB from a sibling who was a perfect HLA match (Gluckman, 2001). Since then, much has been learned about UCB and the role it can play in transplantation. Multiple UCB banks have been established in the United States and Europe. With these and other advances, UCB transplant is a viable option for adult and pediatric HSCT (Ballen, 2005; Laughlin, 2001, 2005).

The use of HSCT has increased for several reasons. First, it allows for the administration of dose-intensive systemic chemotherapy and radiation that would be lethal without transplantation. In addition, HSCT from an allogeneic donor has an additional antitumor effect (AABB et al., 2009). Several characteristics of hematopoietic stem cells make transplantation possible. The first is their ability to regenerate in the marrow. Each hematopoietic stem cell is pluripotent and able to self-replicate, proliferate, and develop into myeloid (red blood cells, platelets, neutrophils, and mac-

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rophages) or lymphoid (T and B lymphocytes) pathways. A small number of stem cells can replicate to repopulate a patient's entire hematopoietic system (AABB et al., 2009). The second characteristic is the cells' ability to find their way to the marrow following IV infusion, a process that is not yet clearly understood (Nuss, Barnes, Fisher, Olson, & Skeens, 2011). The final characteristic of hematopoietic stem cells is that they can be safely cryopreserved, allowing storage for future use (AABB et al., 2009).

## Types of Hematopoietic Stem Cell Transplants

HSCT is categorized based on the origin of the cell source. Categories include autologous, allogeneic, and syngeneic (identical twin). *Autologous* HSCT refers to the use of stem cells collected from a patient, or "self," to be reinfused or "transplanted" at a later date following myeloablation or high-dose chemotherapy. Stem cells are collected and cryopreserved; they may be stored indefinitely until needed for reinfusion at the time of stem cell rescue. If collecting stem cells from the bone marrow, disease-free marrow is desired; when collecting peripheral blood stem cells, this is not a requirement. However, testing for minimal residual disease may be performed on the collected product depending on institutional preferences or protocol requirements (Nuss et al., 2011). Autologous transplantation following myeloablative therapy is used in a variety of diseases, and the goal is to rescue the bone marrow after it has been destroyed by the previous lethal therapy. For some diseases, it is considered part of the initial treatment plan; for others, it is reserved for relapse or persistent disease states. Diseases treated with autologous transplantation include multiple myeloma, non-Hodgkin lymphoma, Hodgkin disease, germ cell tumors, neuroblastoma, brain tumors, sarcomas, acute myeloid and lymphoid leukemias, and recurrent Wilms tumors. Autologous transplantation has expanded to the treatment of autoimmune disorders such as Crohn disease and juvenile rheumatoid arthritis. Clinical trials continue to evaluate the effectiveness of this treatment for other solid tumors, severe autoimmune disease, and some rheumatologic disorders (National Marrow Donor Program [NMDP], n.d.-b). Advantages of autologous transplant include ready access to the stem cells, decreased incidence and severity of side effects, earlier engraftment, and no risk of graft-versus-host disease (GVHD) (Ezzone, 2009; Harris, 2010). However, the risk of potential tumor contamination in the infused cell product and the lack of the immunologic graft-versus-tumor effect may contribute to relapse (Blume & Thomas, 2000; Forman & Nakamura, 2011).

*Allogeneic* HSCT uses a related or unrelated donor as the source of stem cells (see Table 2-2). It is the treatment of choice for patients with cancer who have diseased bone marrow or patients with genetic and immunologic diseases (Forman & Nakamura, 2011) (see Table 2-1). Standard allogeneic transplantation uses myeloablative chemotherapy followed by infusion of stem cells from a compatible donor. Appropriate donors are identified through HLA typing. HLA compatibility is a key factor in predicting transplant-related morbidity and mortality. Because the antigens are genetically acquired, siblings are more likely to have similar HLA-matched stem cells. However, because of the pairing and various combinations of HLA antigens in a family, a patient with one sibling has about a 25% chance of a match. For the average American family, this means there is only a 30% chance of a patient find-

**Table 2-1. Common Diseases Treated With Hematopoietic Stem Cell Transplant**

Type of Disease	Autologous Transplant	Allogeneic Transplant
<b>Malignant</b>		
Hematologic malignancies	Hodgkin disease	Acute lymphocytic leukemia
	Non-Hodgkin lymphoma	Acute myeloid leukemia Chronic myeloid leukemia
Solid tumors	Multiple myeloma	Myelodysplastic syndromes Non-Hodgkin lymphoma Juvenile myelomonocytic leukemia
	Neuroblastoma Sarcoma Germ cell tumors Brain tumors Breast cancer Ovarian cancer Melanoma Lung cancer	–
<b>Nonmalignant</b>		
Hematologic	–	Severe aplastic anemia Fanconi anemia Thalassemia Sickle-cell disease Diamond-Blackfan anemia Chédiak-Higashi syndrome Chronic granulomatous disease Congenital neutropenia
Immunodeficiency	–	Severe combined immunodeficiency disease Wiskott-Aldrich syndrome Functional T-cell deficiency
Genetic	–	Adrenoleukodystrophy Metachromatic leukodystrophy Hurler syndrome Hunter disease Gaucher syndrome
Miscellaneous	–	Osteoporosis Langerhans cell histiocytosis Glycogen storage diseases

Note. Based on information from Ezzone, 2009; Nuss et al., 2011; Pasquini & Wang, 2011.

**Table 2-2. Types of Allogeneic Hematopoietic Stem Cell Transplantation**

Type of Transplant	Cell Source	Advantages	Disadvantages
Syngeneic	Identical twin	No need for immunosuppression	No graft-versus-tumor effect
Matched sibling/ related	Human leukocyte antigen (HLA)-identical relative	No potential stem cell contamination Access to cells because donor is related	Only 25% of population has a sibling match Risk of graft-versus-host disease (GVHD)
Mismatched related	HLA-nonidentical relative	No potential stem cell contamination Increased number of potential donors	Increased risk of GVHD Increased risk of graft failure related to HLA disparity
Matched unrelated	HLA-identical unrelated donor	No potential stem cell contamination	Increased risk of GVHD Limited numbers of non-Caucasian donors Waiting period to identify donor
Mismatched unrelated	HLA-nonidentical unrelated donor	No potential stem cell contamination	Increased risk of GVHD High treatment-related mortality
Umbilical cord blood	Umbilical cord unit	Easy access to cell source	Limited number of cells Delayed time to engraftment Increased infection rates

ing an HLA-matched family donor (Forman & Nakamura, 2011). If an HLA-compatible match is not found in the family, unrelated donors may be sought through bone marrow donor registries or placental cord blood registries, the largest of which is the NMDP (2011c). Advantages to allogeneic HSCT include not only replacement of diseased or damaged stem cells with healthy ones, but also the addition of a powerful immune reaction in which the newly transplanted immune cells may react against any residual disease. This is known as the *graft-versus-tumor effect* (Forman & Nakamura, 2011).

As a result of the immune modulation with allogeneic transplantation, patients are at risk for GVHD, a clinical syndrome that results when immunocompetent donor T lymphocytes recognize and attack minor HLA-related antigens in the recipient or “host” and trigger an immune reaction (Ezzone, 2009; Forman & Nakamura, 2011). GVHD can be acute or chronic (see Chapter 6). It is generally believed that patients undergoing allogeneic HSCT tend to have more complications. Toxicities related to transplant vary depending on conditioning regimen, donor type, level and length of immunosuppression, and organ status prior to transplant (Nuss et al., 2011).

The term *syngeneic* transplant refers to an allogeneic transplant in which stem cells are collected from one identical twin and infused into the other twin following high-dose chemotherapy. The disadvantage of this type of transplant is the lack of graft-versus-tumor effect.

Collection of stem cells from UCB for cord blood transplantation has been gaining interest in recent years. UCB is a rich source of stem cells collected at the time of childbirth that have the ability to induce engraftment in some children and adults. Because the cells from UCB have not matured immunologically, they may be used in transplants where a true HLA match cannot be obtained, such as when there is

no matching sibling donor or no donor match found in a transplant registry (Forman & Nakamura, 2011). The UCB stem cells can be frozen and stored or saved through a cord blood bank to be used in the unrelated registry.

### Nonmyeloablative Hematopoietic Stem Cell Transplantation

Because of the potential dangers of allogeneic HSCT, it traditionally has been reserved for patients younger than age 60 without comorbidities. However, today more transplants are being performed in older patients because of advances in the field (NMDP, n.d.-b). Evidence suggests that the dose-intensive chemotherapy previously thought to be the curative agent in allogeneic HSCT may not be solely responsible for patients’ durable remissions. Rather, the powerful graft-versus-tumor effect may be concurrently responsible for remissions (Forman & Nakamura, 2011; Porter, Roth, McGarigle, Ferrara, & Antin, 1994). It is upon this principle that newer, potentially safer, ways to perform these transplants have been developed.

Nonmyeloablative allogeneic HSCT, a treatment using standard doses of chemotherapy followed by infusions of donor stem cells, has been developed in an effort to take advantage of the graft-versus-tumor effect while providing an effective yet less toxic modality for performing allogeneic HSCT. Results of published studies demonstrate that allogeneic HSCT following nonmyeloablative conditioning has significant activity in patients with chronic myeloid leukemia, acute myeloid leukemia, low-grade lymphoma, and mantle cell lymphoma (Forman & Nakamura, 2011). Ongoing research is also looking at effectiveness in other solid tumors. Nonmyeloablative therapy is under investigation as a method of consolidating remissions in treating patients who are ineligible for standard allogeneic

ic HSCT and for salvaging patients after relapse from previous autologous HSCT.

## Sources of Stem Cells

Stem cells may be collected from the bone marrow, peripheral blood, or UCB. Each of these sources has several advantages and disadvantages. Traditionally, bone marrow was the exclusive source of stem cells. When cells are collected or harbored from bone marrow, the donor is placed under general or epidural anesthesia in an operating room. Bone marrow is obtained by performing multiple needle aspirations of marrow from the posterior or anterior iliac crests. If an inadequate number of cells are harvested, the anterior iliac crests and sternum may be used (AABB et al., 2009; Harris, 2010). The bone marrow is mixed with anticoagulant and filtered to remove bone chips, fat cells, blood clots, and cellular debris. According to AABB et al. (2009), the filtered marrow contains “mature red cells, white cells, platelets, committed progenitors of all lineages, mast cells, fat cells, plasma cells, and pluripotent hematopoietic cells” (p. 3). If the donor and recipient are not ABO compatible, the red blood cells can be removed from the collected marrow, thus avoiding the problem of red cell lysis after infusion of the marrow (Forman & Nakamura, 2011).

Advantages to bone marrow collection are that it can be completed in several hours and is generally well tolerated by the donor; therefore, it may be performed as an outpatient procedure or require only a one-night stay. Maybe more significant is the finding that the use of bone marrow may result in a decreased risk of GVHD, which may have a profound impact on the recipient’s long-term outcome and quality of life (Nuss et al., 2011). For diseases that do not require graft-versus-tumor effect, such as aplastic anemia, sickle-cell disease, or metabolic disorders, many consider it advantageous to use bone marrow. Disadvantages include the need for general or epidural anesthesia and the risk of infection, bleeding, and bone damage (Nuss et al., 2011).

During the past 15 years, the use of peripheral blood stem cells (PBSCs) as a rescue following myeloablative therapy has increased significantly. PBSCs were initially only used for autologous transplants. However, in recent years, the collection of PBSCs from allogeneic donors has grown. Currently, 70% of adults receive PBSCs during transplantation (Karanes et al., 2008).

Stem cells are “mobilized,” or moved out of the bone marrow into the peripheral blood, with the use of granulocyte–colony-stimulating factor (G-CSF) or granulocyte macrophage–colony-stimulating factor (GM-CSF) with or without chemotherapy (Ezzone, 2009; Kröger & Zander, 2002). Typically, an allogeneic donor will be given growth factors for four to six days (Nuss et al., 2011), and as the cells are mobilized into the bloodstream, they can then be collected from the peripheral blood by a process called *apheresis* (Ezzone, 2009). If chemotherapy is used to mobilize stem cells, apheresis will be performed once recovery of peripheral

blood counts has begun, usually 10–16 days after the chemotherapy was administered (Ezzone, 2009).

Apheresis uses centrifugation to remove stem cells from the blood, with the remaining components of the blood remixed and returned to the donor. In autologous transplants, the donor may receive mobilization chemotherapy followed by G-CSF or GM-CSF. Once the stem cells are obtained, they then are mixed with an anticoagulant and a preservative and cryopreserved. In the allogeneic setting, where fresh stem cells are used, the cells usually are not cryopreserved. Instead, the stem cells are infused “fresh” into the transplant recipient (AABB et al., 2009). The cells can be processed to remove ABO-incompatible red cells, ABO-incompatible plasma, or donor T lymphocytes if required (AABB et al., 2009). The number of cells that have the stem cell marker (the CD34 antigen or CD34+) will determine whether enough stem cells were collected. Forman and Nakamura (2011) reported that to have an adequate amount of cells for engraftment, a minimum of  $2 \times 10^6$  CD34 cells/kg body weight must be collected.

One advantage of PBSC collection is that it can be performed as an outpatient procedure with no need for anesthesia, and generally donors of all ages tolerate the procedure well. Most pediatric centers use a cutoff of 18 kg for safely pheresing allogeneic donors because of the potential exposure to blood products. Another important advantage is that cells obtained from the blood are more mature and engraft earlier than cells obtained from bone marrow (Bensinger et al., 1996; Harris, 2010). This quicker hematologic recovery time has many advantages, including fewer infections and decreased length of neutropenia, use of antibiotics, length of thrombocytopenia, risk of bleeding, use of blood products, and organ toxicity. All of these lead to shorter hospital stays and lower costs.

An important consideration is to determine how the PBSCs will be collected. Tunneled multilumen apheresis catheters are inserted into autologous patients for stem cell collection and may stay in place throughout the transplant process. Otherwise, a percutaneous nontunneled “dialysis” catheter can be placed in a central vein for the procedure. Peripheral IV access usually is used for allogeneic donors if good venous access is available and the patient can tolerate this for the duration of the apheresis procedure. Stem cell collection may take one to three or more apheresis procedures over several days, with each procedure lasting four to six hours (Forman & Nakamura, 2011; Harris, 2010).

Collection of UCB units has become more common in recent years. Harvesting cord blood units involves collecting stem cells from an umbilical cord and placenta immediately following birth (AABB et al., 2009). UCB is rich with hematopoietic stem cells. The cord blood is HLA-typed, cryopreserved, and stored in a cord blood bank. There are cord blood banks throughout the world. Advantages include easy access to the cord blood units, the speed with which a cord blood unit can be obtained once selected, and a simple collection procedure with no risk to the mother or child. Additional advantages over unrelated BMT are a lower risk of

GVHD and rejection and decreased rate of virus transmission (Lane, 2005). There is also more room for HLA disparity because the hematopoietic progenitor cells are naïve and have not been exposed to specific antigens; therefore, immunoreactivity with the host is reduced (NMDP, 2011a; Nuss et al., 2011). Disadvantages include the potential for passing genetic diseases to the recipient, a limited and finite number of cells, slower engraftment (cells take time to mature), delayed post-transplant immune reconstitution, and decreased graft-versus-tumor effect. It is also impossible to go back to the donor if additional cells are needed, and the risk of graft failure is greater (Lane, 2005). In UCB transplants, the cell dose is a more important determinant of outcome and survival than the cell source (Nuss et al., 2011).

## National Marrow Donor Program

For the 70% of patients who do not have an HLA-compatible related donor, registries such as the NMDP provide potential unrelated donor options. The NMDP was founded in 1986 and is the world's largest single database of unrelated marrow, cord blood units, and stem cell donors. It contains more than nine million committed volunteer donors and 145,000 cord blood units. Through the NMDP, approximately 5,200 transplants are performed per year. Up to 40% of the facilitated transplants involve an international recipient or donor. With a mission to facilitate unrelated marrow transplantation and PBSCT, NMDP offers a single point of access to finding unrelated marrow, blood stem cells, and cord blood units. Since its inception, NMDP has facilitated approximately 43,000 transplants for patients with blood disorders (e.g., leukemia, aplastic anemia) as well as certain genetic and immune system disorders. At any point in time, approximately 3,000 patients are actively being searched in the registry (NMDP, 2011c).

NMDP initiatives include research (comprehensive database), patient empowerment (Office of Patient Advocacy), educating medical professionals, and working to reduce the time needed for a donor search and the time between finding the donor and the actual transplant. Donor recruitment is a priority. Although Caucasians are well represented on the registries, powerful initiatives are under way for targeted minority recruitment. Efforts are focused on African Americans, American Indians/Alaska Natives, Asian/Pacific Islanders, and Hispanics/Latinos.

The initial step to finding an adult unrelated donor is to obtain the patient's HLA typing using the recommended molecular (DNA) testing methods. The search to find a donor may take several weeks to several months, although searching cord blood banks can reveal blood units that are available immediately. A preliminary search is performed. The preliminary search is a "single snapshot" of potential donors on the registry. It is a computerized search of all stem cell donors and cord blood unit information contained in the registry the day the search is performed. The preliminary search is free, and results usually are available within 24 hours. The search can be performed for any phy-

sician, by the NMDP, or by an NMDP-approved transplant center. After the preliminary search is completed, patients and physicians receive information about unrelated donor transplantation from the NMDP's Office of Patient Advocacy (NMDP, 2011b).

If the decision is made to proceed with the transplant process, the patient must then be referred to an NMDP-approved transplant center. A formal search is then initiated. Formal searches include further laboratory testing performed at the transplant center. This testing is done to confirm the initial HLA results as well as potential matches. Once a donor is identified and the typing is confirmed to be an appropriate match with the patient, the transplant center's physicians may request that the donor proceed to the work-up phase. The volunteer donor will be contacted and educated about the donation process for the stem cell product that has been requested (bone marrow or PBSC). The potential donor will undergo a comprehensive physical evaluation, including blood work and any additional medical testing deemed necessary for safe procurement of the blood cell product (NMDP, 2011b).

The goal of this evaluation is to protect the safety of both the donor and the recipient. The potential transmission of communicable diseases from the donor to recipient is a serious concern. Therefore, laboratory testing includes complete blood count, electrolytes, and renal, hepatic, and endocrine testing. Infectious disease testing includes hepatitis B, hepatitis C, HIV, cytomegalovirus, herpes simplex virus, syphilis, and human T-lymphotropic virus. The donor will also have blood and Rh typing, HLA testing, and pregnancy testing if applicable. A thorough physical examination and medical history including travel, immunization, and transfusion histories will be obtained (Nuss et al., 2011).

## Preparative Regimens

Many combinations of preparative regimens consisting of chemotherapy, immunotherapy, or radiation therapy are given before transplant. The agents used in preparative regimens vary depending on the type of transplant (allogeneic versus autologous), the disease being treated, and the desired effects of the HSCT. The goals of preparative regimens in traditional (myeloablative) allogeneic transplants include eradicating any malignant disease and suppressing the immune system to prevent graft rejection (Ezzone, 2009; Forman & Nakamura, 2011). In autologous transplants, immunosuppression is not necessary because the host is the source of the new stem cell. Thus, the main goals are to eradicate disease and ablate the bone marrow. The goal of HSCT for treatment of nonmalignant diseases is to provide immunosuppression and bone marrow ablation (Ezzone, 2009).

Preparative regimens have evolved over time as more has been learned about various diseases and their responses to different drugs. Early BMTs used total body irradiation (TBI) alone for conditioning. TBI is the exposure of the entire body to gamma radiation. It is delivered in varying doses, usually to patients with lymphoid malignancies, and may

be given as a single dose or in fractionated doses over three or four days (Harris, 2010). Although TBI can produce immunosuppression, bone marrow ablation, and some anti-tumor effects, it is not entirely effective in eradicating diseased marrow. Therefore, chemotherapy is added to optimize the conditioning regimen (Harris, 2010).

Preparative regimens vary depending on the disease, stem cell source, type of transplant, and goals of conditioning. Preparative regimens can be *myeloablative*, meaning that the patient typically receives high-dose chemotherapy with or without radiation therapy, or *nonmyeloablative*, which are less intensive regimens associated with decreased toxicity. Myeloablative preparative or conditioning regimens may last from two days to more than a week and are used to cleanse the bone marrow by destroying diseased cells and killing or suppressing all other marrow cells, thus causing enough immunosuppression to enable donor cells to engraft (Ezzone, 2009; Harris, 2010). Nonmyeloablative regimens are less toxic because of reduced doses of chemotherapy and TBI and are most often used in older adult patients, patients with comorbid diseases, or patients who need the benefit of the associated graft-versus-tumor effect (Champlin et al., 2001; Ezzone, 2009; Harris, 2010). For examples of preparative regimens, see Chapter 4.

Choice of a preparative or conditioning regimen is largely based on the disease being treated and the goal of therapy. For hematologic and immunodeficiency diseases, high doses of chemotherapy with or without TBI will eradicate stem cells in the bone marrow to make space for engraftment of healthy allogeneic cells. The new donor cells will produce normal white blood cells, red blood cells, and platelets and restore immunity (AABB et al., 2009). The goal of HSCT for hematologic malignancies is to administer high-dose chemotherapy to aggressively treat the disease, followed by the reinfusion of stem cells to rescue the patient from the side effects of myeloablation. In genetic and metabolic disorders, chemotherapy is given to destroy the abnormal cells in the bone marrow. Donor cells are infused and upon engraftment produce adequate amounts of previously deficient enzymes, thus hopefully stopping disease progression and symptoms related to the disorder.

The preparative regimen for nonmyeloablative allogeneic HSCT is different than that for traditional allogeneic HSCT because although the process is similar, the goals are different. Patients are conditioned with chemotherapy and/or radiation. The goal of this preparative regimen is not to eradicate the malignancy; rather, the intent is to provide adequate immune suppression to achieve mixed chimera initially and, ultimately, full donor chimera engraftment of an allogeneic blood cell graft. *Chimerism* is the presence of donor hematopoietic cell lines in the recipient of an allogeneic transplant. This is evaluated by using genetic markers to confirm engraftment and to distinguish the donor from the recipient. The optimal conditioning regimen is yet to be determined. Regimens typically consist of highly immunosuppressive chemotherapeutic agents, such as purine analogs (e.g., fludarabine) or alkylating agents (e.g., busulfan,

cyclophosphamide) in nonmyeloablative doses alone or in combination with immunosuppressive agents (e.g., antithymocyte globulin), monoclonal antibodies (alemtuzumab), or low-dose total nodal irradiation or TBI (200 cGy). The combination of chemotherapy, radiation, and immunotherapy is intended to suppress the immune system of the host and allow engraftment of donor cells, as well as induce a graft-versus-tumor response in which the donor's immune cells attack the host malignancy (Nuss et al., 2011). For additional information on preparative regimens, see Chapter 4.

## Clinical Evaluation

Because many life-threatening complications are associated with HSCT, the decision to use this treatment is based on a thorough evaluation of the patient. Some variation exists among transplant centers in terms of eligibility requirements, diseases treated, and components of the pretransplant clinical evaluation. In an effort to standardize as well as promote quality medical practices, the Foundation for the Accreditation of Cellular Therapy (FACT) was formed in 1996 by the American Society for Blood and Marrow Transplantation and the International Society for Cellular Therapy (FACT, 2011). FACT is a national voluntary inspection and accreditation program that encompasses all phases of hematopoietic cell collection, processing, and transplantation. It was developed to oversee and encourage standardization of quality practices in transplant centers. Centers that meet rigorous standards of quality medical care and laboratory practice are recognized with certificates of accreditation. FACT requirements for patient evaluation are indicated in Figure 2-1.

General considerations for eligibility include determining that the patient has chemotherapy-sensitive disease, adequate organ function, and no life-threatening viral exposures or comorbidities. Additionally, the patient's age, performance status, and ability to comply with treatment are considered. A clinical evaluation, including a complete health history documenting the history of the present illness, should be obtained. Information should include the disease and treatment course from diagnosis to the time of transplant. A general health history, including past medical and surgical history and family, social, and travel history, should be obtained, along with documentation of allergies, medications, and, if female, gynecologic history. A complete physical examination should be performed, including laboratory studies and diagnostics assessing vital organ function and infectious disease testing (FACT, 2011).

In addition to the clinical assessment, a psychosocial assessment of the patient and family should be performed (Nuss et al., 2011). The patient should be evaluated for comprehension of the procedure, potential risks, side effects, and complications and ability to comply with therapy. Psychosocial evaluation should include social and spiritual issues, psychological well-being, financial issues, and family concerns. Children should have neuropsychological testing performed to have a baseline for further assessments.

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## Figure 2-1. Clinical Evaluation Requirements for Transplant

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### Laboratory Evaluation

- Complete blood count with differential
- Chemistry profile
- Electrolytes, liver function tests, blood urea nitrogen/creatinine, prothrombin time/partial thromboplastin time, international normalized ratio
- Hepatitis B surface antigen<sup>a,b</sup>
- Hepatitis C antibody<sup>a,b</sup>
- HIV antibody<sup>a,b</sup>
- HIV1/2 antibody<sup>a,b</sup>
- Human T-cell leukemia virus 1<sup>a,b</sup>
- Rapid plasma reagin test<sup>a,b</sup>
- Cytomegalovirus immunoglobulin G (IgG), IgM<sup>a,b</sup>
- Herpes simplex virus IgG
- ABO/Rh<sup>a,b</sup>
- Human leukocyte antigen typing for allogeneic transplants<sup>b</sup>
- Toxoplasmosis antibody
- Cocci serologies
- Varicella zoster virus IgG
- Glomerular filtration rate/creatinine clearance
- Pregnancy test<sup>a,b</sup>

### Organ Function Testing

- Multigated acquisition scan/echocardiogram
- Pulmonary function test
- 12-lead electrocardiogram
- Dental examination

### Disease Evaluation

- Bone marrow aspirates and biopsies
- Lumbar puncture
- Computed tomography scans
- Magnetic resonance imaging
- Bone scan
- Gallium scan
- Positron-emission tomography scan
- Tumor markers
- 24-hour urine protein electrophoresis
- Immunoglobulins
- Urine catecholamines (vanillylmandelic acid/homovanillic acid)

<sup>a</sup> Required by Foundation for the Accreditation of Cellular Therapy; <sup>b</sup> Required for donor also

*Note.* Based on information from Foundation for the Accreditation of Cellular Therapy, 2011.

Finally, consent must be obtained prior to HSCT. If the patient is a minor, a parent or guardian must consent; however, children younger than 18 years of age may sign an assent form.

Allogeneic transplant donors must undergo a thorough clinical evaluation and psychosocial assessment. The donor should have a complete medical history and physical examination to rule out genetic or infectious diseases and significant health problems that may pose a risk to either the patient or the donor during the collection of stem cells (see Figure 2-1). The stem cell donor evaluation is described in detail in Chapter 3. Psychological intervention allows the donor to express any fears he or she has regarding collection of stem cells or bone marrow and discuss ways to cope

with those fears. Intervention should be provided to assist donors in processing feelings of guilt or anxiety related to the transplant recipient's outcome. The identity of an unrelated donor is typically kept confidential for at least one year. Some centers allow recipients to have anonymous contact with their donor during the first year via letters or cards; some allow direct contact one or more years after transplant if both the donor and recipient consent; and some do not allow any contact (NMDP, n.d.-a). Informed consent for the collection of peripheral blood or bone marrow stem cells is obtained prior to donation.

## Patient and Family Education

Transplantation is a very intense and complicated process that requires educational efforts throughout all phases of treatment. Nurses have an excellent opportunity to provide this education to patients, donors, and families or support people at each transplant phase. Education can be done using discussions, written materials, informational Web sites, and audiovisual aids if available. Barriers to learning should be identified and addressed to enhance learning.

Donors should be instructed about the diagnostic studies and laboratory tests required to evaluate their health status prior to donation of stem cells. Donors should have a thorough understanding of the collection process, the potential risks and complications, and the potential outcomes that they may experience, along with the potential outcomes for the recipient of their donated cells. Donors also should know how to seek medical attention if they develop complications or have questions following collection. The donor must sign informed consent papers prior to the collection being performed.

Pretransplant education for patients and families should be individualized and ongoing, with continued evaluation of their comprehension and understanding of this process. Many patients have received other therapies prior to transplant and may have previous experience with chemotherapy or radiation therapy and hospitalization. Assessment of a patient's prior experience with side effects may guide the nurse in providing appropriate pretransplant education. The nurse should discuss the route of administration, dosage, side effects, and administration of all medications, such as chemotherapeutic agents, anti-infectives, immunosuppressives, antiemetics, immunomodulators, analgesics, and growth factors. Information should be provided regarding the actual reinfusion and potential side effects and complications occurring during aplasia, including organ toxicity, infection, and bleeding. For patients undergoing allogeneic HSCT, education should include the risks, clinical presentation, and treatments for GVHD and hematopoietic growth factors. Additionally, the potential side effects of immunosuppressive medications, such as high risk of infection, hepatotoxicity, and nephrotoxicity, should be discussed.

Because of the level of caregiver burden for families and support people of patients undergoing HSCT, family structure and function should be assessed early in the transplant

process. Many transplant centers require a competent adult caregiver to be identified prior to initiation of transplant, especially if most of the care is to occur in the ambulatory setting as in autologous or nonmyeloablative transplants. Efforts should include educating families in both the physical and psychosocial elements of this process. Helping families to identify key support people and teaching them to delegate activities to maximize available resources is a key element in managing caregiver burden. Family members should be encouraged to express their fears and concerns regarding the possibility of death of the patient and their expectations and hope for a positive outcome. Patients and families need to be aware that transplant may not be curative. Nurses, social workers, and psychosocial staff should address these issues and acknowledge changing roles within the family and their impact on the HSCT process. Whenever possible, families and support people should be encouraged to participate in groups and use other available support networks.

The education of a child undergoing transplantation requires special attention. Many pediatric transplant centers employ child life specialists who can assist with developing appropriate education. Educational efforts should be directed toward the child's developmental stage (Nuss et al., 2011). Although children may not understand everything, an attempt should be made to help them understand why they are in the hospital, what is going to happen, how they may feel, and what they can do during the transplant process. Teaching should be conducted at appropriate times, and children should always be told what to expect prior to procedures or administration of medications. Children should be given the opportunity to ask questions and to share their concerns. Parents may need help in addressing their children's questions or needs. Child life specialists, nurses, and other staff should be available to assist with education of children and families (Nuss et al., 2011).

Much of the basics of PBSCT and BMT can be applied to both adults and children. However, special considerations exist for children. Pediatric patients have unique growth and developmental needs. Children's ability to cope will be dependent upon their developmental level along with the trust and support they feel from the family and the transplant staff (Secola, 1997). Children should have opportunities to have their emotional and developmental needs met. This could include things such as enabling them to continue schoolwork, activities, play, and exercise, if possible. Peer interaction should be continued via computers, videophones, and letters, if age appropriate. Social interaction with family, friends, and staff will be very important. Staff who are familiar with pediatric patients and their needs should be involved in the care of these patients when at all possible. Family involvement is crucial when a child is undergoing the transplant experience, and the entire family will need to be cared for and included.

Finally, discharge education is very important and should be initiated early to optimize planning and resources. Because of the high level of anxiety of patients and caregiv-

ers, information should be presented clearly and reinforced frequently during the hospital stay. Discharge instructions should be explained verbally by the nurse and reinforced by providing printed materials to take home and should be realistic regarding life after transplant (Boyle et al., 2000). Information provided should include the risk of infection, practices to prevent infection, physical activity expectations and restrictions, and medication administration. The patient and caregiver need information on how to meet daily nutritional requirements to combat fatigue. The possibility of GVHD and long-term complications of each organ system should be addressed. A follow-up plan should be outlined for the patient and family.

Discharge teaching should include family members and support people. Family roles may change throughout the transplant process as the patient requires changing levels of support. Family members should be instructed in ways to cope with the stress associated with this dynamic process (Wochna, 1997). Everyday family life may be disrupted with frequent follow-up office visits in addition to the long-term effects of treatment (e.g., fatigue, GVHD). The family also may be dealing with financial issues, uncertainty about the future, fear of relapse, and fear of death (Rivera, 1997). Recurrence anxiety is a predominant theme rarely addressed by the professional team because the assessment of symptoms and recovery from transplant take priority (Boyle et al., 2000). The family should be given time to discuss all of these issues and express any concerns prior to the patient's discharge so that a follow-up plan can be cooperatively developed.

## Conclusion

HSCT is a very complex process that continues to grow and develop. It is essential for nurses to maintain current knowledge of the basics so that they can continually improve the quality of care provided to patients and families. Treatment advances are occurring rapidly, and nurses have a tremendous opportunity to prepare and assist patients throughout the transplant process.

## References

- AABB, American Association of Tissue Banks, American Red Cross, American Society for Blood and Marrow Transplantation, America's Blood Centers, American Society for Apheresis, ... National Marrow Donor Program. (2009). Circular of information for the use of cellular therapy products. Retrieved from [http://www.aabb.org/resources/bct/Documents/coi\\_ct1109.pdf](http://www.aabb.org/resources/bct/Documents/coi_ct1109.pdf)
- Appelbaum, F.R. (1996). The use of bone marrow and peripheral blood stem cell transplantation in the treatment of cancer. *CA: A Cancer Journal for Clinicians*, 46, 142-164. doi:10.3322/canjclin.46.3.142
- Ballen, K.K. (2005). New trends in umbilical cord blood transplantation. *Blood*, 105, 3786-3792. doi:10.1182/blood-2004-10-4125
- Bensinger, W.I., Clift, R., Martin, P., Appelbaum, F.R., Demirer, T., Gooley, T., ... Buckner, C.D. (1996). Allogeneic peripheral blood stem cell transplantation in patients with advanced hematologic malignancies: A retrospective comparison with marrow transplantation. *Blood*, 88, 2794-2800.
- Blume, K.G., & Thomas, E.D. (2000). A review of autologous hematopoietic cell transplantation. *Biology of Blood and Marrow Transplantation*, 6, 1-12. doi:10.1016/S1083-8791(00)70047-4

- Boyle, D., Blodgett, L., Gnesdiloff, S., White, J., Bamford, A., Sheridan, M., & Beveridge, R. (2000). Caregiver quality of life after autologous bone marrow transplantation. *Cancer Nursing, 23*, 193–203. doi:10.1097/00002820-200006000-00006
- Champlin, R., Khouri, I., Anderlinie, P., Gajewski, J., Kornblau, S., Moll-drem, J., ... Giralt, S. (2001). Nonmyeloablative preparative regimens for allogeneic hematopoietic transplantation. *Bone Marrow Transplantation, 27*(Suppl. 2), S13–S22. doi:10.1038/sj.bmt.1702864
- Duncombe, A. (1997). ABC of clinical haematology: Bone marrow and stem cell transplantation. *BMJ, 314*, 1179–1182. doi:10.1136/bmj.314.7088.1179
- Ezzone, S.A. (2009). Blood and marrow transplantation. In B.H. Gobel, S. Triest-Robertson, & W.H. Vogel (Eds.), *Advanced oncology nursing certification review and resource manual* (pp. 261–303). Pittsburgh, PA: Oncology Nursing Society.
- Forman, S.J., & Nakamura, R. (2011). Hematopoietic cell transplantation. In R. Pazdur, L.D. Wagman, K.A. Camphausen, & W.J. Hoskins (Eds.), *Cancer management: A multidisciplinary approach: Medical, surgical, and radiation oncology* [Online edition]. Retrieved from <http://www.cancer-network.com/cancer-management/hematopoietic-cell-transplantation/article/10165/1802824?pageNumber=1>
- Foundation for the Accreditation of Cellular Therapy. (2011). *FACT-JACIE international standards for cellular therapy product collection, processing, and administration* (4th ed.). Lincoln, NE: University of Nebraska.
- Gluckman, E. (2001). Hematopoietic stem-cell transplants using umbilical-cord blood. *New England Journal of Medicine, 344*, 1860–1861. doi:10.1056/NEJM200106143442410
- Harris, D.J. (2010). Transplantation. In J. Eggert (Ed.), *Cancer basics* (pp. 317–342). Pittsburgh, PA: Oncology Nursing Society.
- Karanes, C., Nelson, G.O., Chitphakdithai, P., Agura, E., Ballen, K.K., Bolan, C.D., ... Confer, D.L. (2008). Twenty years of unrelated donor hematopoietic cell transplantation for adult recipients facilitated by the National Marrow Donor Program. *Biology of Blood and Marrow Transplantation, 14*(Suppl. 9), 8–15. doi:10.1016/j.bbmt.2008.06.006
- Kröger, N., & Zander, A.R. (2002). Dose and schedule effect of G-CSF for stem cell mobilization in healthy donors for allogeneic transplantation. *Leukemia and Lymphoma, 43*, 1391–1394. doi:10.1080/10428190290033323
- Lane, T.A. (2005). Umbilical cord blood grafts for hematopoietic transplantation in adults: A cup half empty or half full? *Transfusion, 45*, 1027–1034. doi:10.1111/j.1537-2995.2005.05120.x
- Laughlin, M.J. (2001). Umbilical cord blood for allogeneic transplantation in children and adults. *Bone Marrow Transplantation, 27*, 1–6. doi:10.1038/sj.bmt.1702740
- Laughlin, M.J. (2005). Transplantation of 2 UCB units in adults (Comment). *Blood, 105*, 915–916. doi:10.1182/blood-2004-11-4300
- Lorenz, E., Uphoff, D., Reid, T.R., & Shelton, E. (1951). Modification of irradiation injury in mice and guinea pigs by bone marrow injections. *Journal of the National Cancer Institute, 12*, 197–201.
- Main, J.M., & Prehn, R.T. (1955). Successful skin homografts after the administration of high dosage x radiation and homologous bone marrow. *Journal of the National Cancer Institute, 15*, 1023–1029.
- National Marrow Donor Program. (2011a). Hematopoietic cell sources tailored to the patient. Retrieved from [http://marrow.org/Physicians/Transplant\\_Advances/Expanded\\_Cell\\_Sources.aspx](http://marrow.org/Physicians/Transplant_Advances/Expanded_Cell_Sources.aspx)
- National Marrow Donor Program. (2011b). Unrelated donor search process: Step by step. Retrieved from [http://marrow.org/Physicians/Unrelated\\_Search\\_and\\_Transplant/Donor\\_or\\_CBU\\_Search/Search\\_step\\_by\\_step.aspx](http://marrow.org/Physicians/Unrelated_Search_and_Transplant/Donor_or_CBU_Search/Search_step_by_step.aspx)
- National Marrow Donor Program. (2011c). Who we are—About the National Marrow Donor Program and Be The Match. Retrieved from [http://marrow.org/About/Who\\_We\\_Are/Who\\_We\\_Are.aspx](http://marrow.org/About/Who_We_Are/Who_We_Are.aspx)
- National Marrow Donor Program. (n.d.-a). Contact with your donor after transplant. Retrieved from [http://marrow.org/Patient/Transplant\\_Process/Contact\\_with\\_Your\\_Donor\\_after\\_Transplant.aspx](http://marrow.org/Patient/Transplant_Process/Contact_with_Your_Donor_after_Transplant.aspx)
- National Marrow Donor Program. (n.d.-b). Expanded patient selection. Retrieved from [http://marrow.org/Physicians/Transplant\\_Advances/Patient\\_Selection.aspx](http://marrow.org/Physicians/Transplant_Advances/Patient_Selection.aspx)
- Nuss, S., Barnes, Y., Fisher, V., Olson, E., & Skeens, M. (2011). Hematopoietic cell transplantation. In C. Baggott, D. Fochtman, G.V. Foley, & K.P. Kelly (Eds.), *Nursing care of children and adolescents with cancer and blood disorders* (4th ed., pp. 405–466). Glenview, IL: Association of Pediatric Hematology/Oncology Nurses.
- Pasquini, M.C., & Wang, Z. (2011). Current use and outcome of hematopoietic stem cell transplantation: CIBMTR summary slides, 2011. Retrieved from <http://www.cibmtr.org>
- Porter, D.L., Roth, M.S., McGarigle, C., Ferrara, J., & Antin, J.H. (1994). Induction of graft-versus-host disease as immunotherapy for relapsed chronic myeloid leukemia. *New England Journal of Medicine, 330*, 100–106. doi:10.1056/NEJM199401133300204
- Rivera, L.M. (1997). Blood cell transplantation: Its impact on one family. *Seminars in Oncology Nursing, 13*, 194–199. doi:10.1016/S0749-2081(97)80035-6
- Secola, R. (1997). Pediatric blood cell transplantation. *Seminars in Oncology Nursing, 13*, 184–193. doi:10.1016/S0749-2081(97)80034-4
- Thomas, E.D. (1995). Transplantation of hematopoietic progenitor cells with emphasis on the results in children. *Turkish Journal of Pediatrics, 37*, 31–43.
- Wohna, V. (1997). Anxiety, needs, and coping in family members of the bone marrow transplant patient. *Cancer Nursing, 20*, 244–250. doi:10.1097/00002820-199708000-00003