

An Overview of Stem Cell Transplant as a Treatment for Cancer

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The National Cancer Institute estimates that 10.1 million Americans have a history of cancer, and that three of every four American families will have at least one family member diagnosed with the disease (National Cancer Institute, 2006). Stem cell transplantation (SCT) has been used for over 50 years (Kolb, Gidwani, & Grupp, 2006) to treat a multitude of cancers and non-myelodysplastic diseases after patients have completed standard treatment regimes. SCT usually is used to treat hematologic and lymphoid cancers, such as acute lymphocytic leukemia, acute myelogenous leukemia, chronic myelogenous leukemia, Hodgkin's disease, multiple myelo-

ma, and non-Hodgkin's lymphoma (Copelan, 2006). Transplantation early in the course of the disease is critical in patients with hematologic cancers (Copelan, 2006). Every year thousands of patients undergo SCT to "rescue" them from high-dose chemotherapy, which ablates the bone marrow (Ball, 2003). Other disease entities that are now being treated with SCT include genetic diseases, acquired anemias, germ cell tumors, primary amyloidosis, myelodysplastic diseases, neuroectodermal tumors and ependymoma, ovarian cancer and germ cell tumors arising in the ovaries, solid tumors of childhood, and other diseases classified as rare diseases (Copelan, 2006; Kolb et al., 2006).

Additionally, SCT is still considered investigational for numerous non-malignant autoimmune diseases such as lupus, but may offer a cure or a better quality of life (Burt et al., 2006; Petri & Brodsky, 2006).

Because many medical-surgical nurses will come in contact with SCT patients before and after the actual transplants (and perhaps due to staffing shortages within specialized transplant units), stem cell use in combating malignancy and the nurse's role in the process will be described. Nursing care and the complexity of this care continue to change, and nurses must respond to and reassess the need for practice changes constantly to provide high-quality care.

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Overview

Stem cell transplant consists of the transfer of hematopoietic stem cells after the administration of high-dose chemotherapy, with or without radiotherapy. The chemotherapy/radiotherapy destroys malignant cells — and eradicates the patient's bone marrow in the process. SCT is used to “rescue” the patient and re-establish the bone marrow. The source of hematopoietic stem cells can be either bone marrow or peripheral blood.

Fetal blood harvested from the placenta and umbilical cord, referred to as *cord blood*, is also a stem cell source. Cord blood contains a significant number of hematopoietic stem cells. Using umbilical cord blood gives the opportunity of a larger donor pool because donors do not have to be matched as closely as bone marrow or peripheral blood donors, and there is no risk or discomfort to the donor. The risk of graft-versus-host disease (GVHD), which occurs when the immune cells from a donor attack the tissues of the person receiving the transplant, also is significantly lower (Kolb et al., 2006; Slavin et al., 1998).

Three basic types of SCTs exist: *autologous* (self donor), *allogeneic* (from a donor other than self), and *syngeneic* (identical twin is the donor) (Ljungman et al., 2006). Autologous stem cell support/transplantation (previously referred to as an *autologous bone marrow transplant*) consists of the intravenous reinfusion of the patient's own stem cells, which were harvested previously. Autologous stem cells can be harvested from bone marrow or from circulating blood through the process of apheresis. Because this type of transplantation uses the patient's own cells, there is no risk that the immune system will reject the transplant or that the transplanted cells will attack the patient's body. A possible disadvantage is that cancer cells may be harvested along with the stem cells and then reinfused

Table 1.
Where Do Stem Cells Come From?

Embryonic stem cells compose the inner cell mass of the blastocyst during fetal development. Initial hematopoiesis takes place during early embryogenesis at approximately 3-4 weeks post-fertilization (Brunstein & Verfaile, 2004). By the 20th week of fetal development, the bone marrow is producing all cells of the eight major cell lines of hematopoiesis (Metcalf, 1998). All variants of human cells start as a pluripotent stem cell, which have the unique ability to self-replicate and produce multilineage cells (Wujcik, 1997). Stem cells can be found in various tissues in the adult body, such as the bone marrow within the sternum, ribs, long bones, and the iliac crests. Stem cells also can be obtained from sources like the umbilical cord of a newborn baby (Chouinard & Finn, 2007).

back into the body. See Table 1 to learn where stem cells come from.

Allogeneic SCT is the administration of blood or marrow stem cells from another person, usually a sibling whose human leukocyte antigens match those of the patient. On occasion, a haploidentical relative or a matched unrelated donor can be located from the National Donor Bank, although finding a match for certain racial/ethnic groups can be difficult because of the comparatively small numbers of potential minority donors in the National Donor Bank. The advantage of allogeneic SCT is that the donor stem cells produce their own immune cells, which may help destroy any cancer cells that remain after high-dose treatment. This is called the *graft-versus-malignancy effect* (McSweeney et al., 2001). However, several possible drawbacks to allogeneic SCT exist, including failure to engraft, donor cell death, or GVHD.

Syngeneic SCT is a special kind of allogeneic transplant. The donor is an identical twin with identical tissue types; therefore GVHD is not a problem in this type of transplant. Because few people are identical twins, this type of transplant is very rare. Table 2 shows different types of stem cell transplants.

Autologous Versus Allogeneic

Regardless of the type of SCT, the procedure can be difficult and risky, and the mortality rate after

stem cell transplantation is approximately 12% in the first 100 days (Ball, 2003). Numerous causes related to mortality exist, including GVHD, pneumonia, infection, and organ failure. The choice to use autologous versus allogeneic transplant is dependent on many things, including the availability of a haploidentical matched donor, the individual disease, the age of the patient, and the remission status of the cancer (Ezzone & Pokorny, 2007).

Because autologous SCT recipients do not experience acute or chronic GVHD, their quality of life might be assumed to be superior to that of allogeneic transplant patients. However, the chemotherapy agents associated with autologous transplants can have long-lasting cardiopulmonary, immunosuppressive, renal, and other side effects that affect quality of life (Buchsel & Whedon, 1995). The most worrisome side effect of autologous transplantation is treatment-related malignancy. With both autologous and allogeneic transplantation, damage to vital organs and additional problems, such as osteoporosis, chronic GVHD, and immunologic and endocrine complications, are now recognized as post-transplant related complications (Antin, 2002).

For patients who receive an allogeneic bone marrow transplant as treatment for acute myelogenous or lymphoblastic leukemia,

Table 2.
Types of Stem Cell Transplants

	Autologous	Allogeneic	Syngeneic
Donor	Patient	Another person	Identical twin to patient
Usual Source of Stem Cells	Bloodstream	Bone marrow	Bone marrow
Average Length of Hospital Stay	4-8 weeks	4-8 weeks Usually an additional 100-120 days as an outpatient	4-8 weeks
Often Used to Treat	Non-Hodgkin's lymphoma Hodgkin's disease Multiple myeloma Acute and chronic leukemias Solid tumors of childhood Other solid tumors (ovarian cancer, sarcoma, germ cell tumor, etc.) Neuroblastoma Medulloblastoma Autoimmune disorders Amyloidosis	Leukemias: acute and chronic, lymphocytic and myelogenous Non-Hodgkin's lymphoma Hodgkin's disease Myelodysplastic syndrome Acquired anemias Multiple myeloma Severe combined immunodeficiency disorder Thalassemia major Wiskott-Aldrich syndrome Autoimmune disorders	All listed for autologous and allogeneic transplants

Sources: Adapted from Kolb, Gidwani, & Grupp, 2006.

chronic myelogenous leukemia, or aplastic anemia, and who are free of their original disease 2 years later, the disease is probably cured (Socié et al., 1999). However, for many years after transplantation, the mortality among these patients is higher than in a normal population. Therefore, allogeneic transplant typically has been limited to younger and more medically fit patients, with therapy limited to hospital inpatient specialized transplant units (McSweeney et al., 2001).

The Transplant Process and What to Expect

It is beyond the scope of this column to discuss all the specifics of the various types of SCT; however, the recommended reading list provides additional references concerning allogeneic and syngeneic transplant. The remainder of this column will concentrate on the autologous SCT process and the needs of patients treated with autologous SCT, because these are the

types of patients that medical-surgical nurses will encounter most often. Table 3 provides some definitions at a glance.

Autologous transplants are relatively safe procedures, with low rates of complications and infections compared with allogeneic transplants. Armitage and Antman (1992) reported transplant-related mortality rates in community cancer centers similar to those observed in patients treated in specialized transplant centers. The continuity of care established with the treating oncologist, nurses, and personnel of the local hospital was determined to be a major advantage, as was the patient's existing support system (Weaver, West, Schwartzberg, Birch, & Buckner, 1998).

In many instances, most of the procedure can be done on an outpatient basis; this depends on the patient, physician, availability of a patient caregiver, and the generally accepted standards of care in the specific treatment location or

region (Buchsel & Whedon, 1995). Most patients treated with SCT at a tertiary transplant center are required to have a full-time caregiver with them throughout treatment because they are treated as an outpatient while staying in a hotel close to the hospital. The requirement for a full-time caregiver can create multiple hardships on family and friends. Regardless of the facility chosen for SCT, most cancer patients have gone through a fairly arduous treatment process prior to SCT, and may have been admitted to the hospital between cycles of chemotherapy with related complications, such as infection, dehydration, anemia, pain from associated neuropathies, and/or bleeding with associated pancytopenia, or neutropenia. As with other chronically ill people, these patients and their families require the nurse to use excellent communication skills and compassion.

Before the transplant, a complete work up is done. This usually consists of complete blood panels,

Table 3.
Definitions at a Glance

Allogeneic stem cell transplant	A transplant from a human donor who is not an identical genetic match in which bone marrow or peripheral blood stem cells from a donor (usually related) are collected, stored, and infused into a patient (recipient) following high-dose chemotherapy and/or radiation therapy.
Apheresis	Procedure in which blood is taken from a donor. A blood component (such as white blood cells, red blood cells, or plasma) is separated out, and the remaining blood components are infused back into the donor.
Autologous stem cell transplant/rescue	Procedure in which a patient's own stem cells from the bone marrow or peripheral blood are collected, stored, and reinfused following high-dose chemotherapy and/or radiation therapy; sometimes referred to as stem cell rescue because the patient's stem cells "rescue" the patient from the effects of the cancer therapy.
Bone marrow transplant (BMT)	Procedure in which stem cell-containing bone marrow is collected, stored, and infused following high-dose chemotherapy and/or radiation therapy.
Conditioning regimen	Combination of chemotherapy and/or radiation treatments administered over a period of several days prior to stem cell transplantation in order to destroy cancer cells.
Cord blood transplant	Type of transplant in which the stem cells are obtained from the umbilical cord and placenta following the delivery of a baby. These cells are frozen for future use.
Engraftment	The process of infused stem cells moving into the marrow of the patient and producing blood cells of all types. Engraftment is first evident when new white cells, red cells, and platelets begin to appear in the person's blood following stem cell transplantation.
High-dose chemotherapy	Administration of higher, more effective doses of chemotherapy. Because high-dose chemotherapy destroys the bone marrow, a stem cell transplant/rescue is required to replenish blood-forming bone marrow cells.
Mobilization	Administration of colony-stimulating factors or chemotherapy to help move stem cells from the bone marrow into the bloodstream to increase the number of peripheral blood stem cells collected for a stem cell transplant/rescue.
Myeloablation (ablation)	The killing of bone marrow by chemotherapy and/or radiation. This term usually refers to the complete or near-complete destruction of the bone marrow.
Peripheral blood stem cell (PBSC) transplant	Procedure in which blood containing mobilized stem cells are collected by apheresis, stored, and infused following high-dose chemotherapy and/or radiation therapy.
Refractory disease	Disease that has not responded to initial therapy.
Relapsed disease	Disease that initially responded to therapy but has begun to progress again.
Remission	Period during which no evidence of cancer is present.
Responsive disease	Disease that is responding to therapy, with a decrease in malignant cells of at least 50%.
Stable disease	Treatment outcome whereby the disease has either responded to therapy and is stable once treatment is stopped, or has not responded to therapy but has not progressed.
Standard therapy	Treatment that has been shown to be safe and effective in clinical studies and is adopted as standard practice outside of clinical trials.
Stem cell	Parent cell that grows and divides to produce red blood cells, white blood cells, and platelets. Found primarily in the bone marrow, but also in the peripheral blood.
Stem cell transplant	Therapeutic procedure in which bone marrow or peripheral blood stem cells are collected, stored, and infused into a patient following high-dose chemotherapy to restore blood cell production.
Syngeneic stem cell transplant	Procedure in which bone marrow or peripheral blood stem cells from a patient's identical twin are collected, stored, and infused into the patient following high-dose chemotherapy and/or radiation therapy.
Tandem transplant	Type of transplantation technique in which a patient receives two planned transplants within a short period of time.
Total body irradiation (TBI)	Administration of radiation to the entire body with the purpose of destroying tumor cells in preparation for a stem cell transplant.

Sources: Adapted from National Marrow Donor Program, 2006; Rocky Mountain Bone and Marrow Transplant Program, 2006.

including infectious serologies, echocardiogram, electrocardiogram, chest X-ray, pulmonary function test, computed tomography and positron emission tomography scans, ultrasounds, bone scans, marrow aspirates, and biopsies. This evaluation phase is a difficult time for patients and their families. The nursing staff is involved intimately with them to address any questions, helping them understand complex medical information, providing support, and assisting them to understand all the information regarding the transplant process and possible complications (Buchsel & Whedon, 1995).

Once the patient is approved for the procedure, the stem cell harvest usually takes place in an apheresis center over several sessions. Most transplant centers or Comprehensive Cancer Centers have trained nurses or technicians dedicated to performing the apheresis procedure. The process requires placement of an intravenous needle into each of the patient's arms, or the use of a vascular access device that has two lumens (double-lumen central venous catheter) or ports. Both methods provide a route for blood being circulated through the apheresis machine. The side effects of apheresis generally are minimal and usually not more than when donating whole blood or platelets (Buchsel & Whedon, 1995).

To move stem cells from the bone marrow to the bloodstream, *mobilization treatment* takes place. The patient either receives daily injections of a growth factor followed by daily stem cell collections, or chemotherapy followed by daily injections of a growth factor. The process takes approximately 2-4 hours per collection, with four collections as the average required, but some patients may need more collections to acquire an adequate amount of cells (Cancer Treatment Centers of America, 2007; Multiple Myeloma Research Foundation, 2005). An excellent description of

stem cell collection and preconditioning is provided in the reference by Ezzone and Pokorny (2007).

After the cells are collected, a pretransplant *preconditioning phase* begins. The conditioning days are called *minus days* on a timeline to the stem cell/marrow infusion day, which is referred to as *Day Zero*. The patient is treated with the planned conditioning regimen, which may consist of combination chemotherapy alone or chemotherapy and total body irradiation (TBI) (Buchsel & Whedon, 1995). The conditioning regime used against the cancer must be able to eliminate the disease; however, it also ablates the bone marrow. After the conditioning regime, the patient has 1 or 2 days to rest prior to stem cell infusion (Buchsel & Whedon, 1995; Vesole, Simic, & Lazarus, 2001).

On Day Zero, the actual *transplant* or infusion of hematopoietic stem cells occurs. Some patients may react with nausea or vomiting to the dimethyl sulfoxide (DMSO), a chemical preservative added to the stem cells to prevent damage during freezing. Patients should be educated that they may experience a garlic-like taste as the stem cells are reinfused, and the room will have a garlic-like smell from the DMSO that may last 10-24 hours.

The Nurse's Role

During the time around the nadir (when blood counts are at their lowest point) and once the reinfusion has occurred, the patient often will require transfusions of platelets and red cells. The nurse plays a vital role during the time of infusion and the post-infusion period, monitoring the patient's condition with thorough physical assessments and evaluation of vital signs, weight, fluid status, and lab values (Buchsel & Whedon, 1995). The nurse must be vigilant for signs of side effects and complications of the conditioning regimen because early identification of problems can reduce morbidity and mortality for

this very ill patient (Ezzone & Pokorny, 2007).

The recovery period begins the first day after infusion, and the patient may have a few or multiple complications, both physical (for example, pulmonary, cardiac, neurological, renal, hepatic) and emotional. Recovery of normal levels of red blood cells, white blood cells, and platelets, or *engraftment*, usually occurs 8-12 days after the infusion of stem cells. Neutrophils are one of the markers of engraftment; the absolute neutrophil count must be at least 500 for 3 days in a row to say that engraftment has occurred (National Marrow Donor Program, 2005; Vachani, 2005).

After engraftment occurs, blood cell counts continue to rise and the immune system becomes stronger. The patient usually remains under the care and monitoring of the transplant team. He or she often needs 2-3 months to regain energy (St. Vincent Health, 2006), and complete recovery of the immune system normally takes 1-2 years from the time of transplant (Abeloff, Armitage, Niederhuber, Kastan, & McKenna, 2004; Aquino, Aquino, & Ansari, 1999; National Cancer Institute, 2006).

The patient who receives some of the SCT as an inpatient is being discharged earlier from hospitals and receives most of his or her care via ambulatory cancer centers. Many treatments, such as administration of blood products, intravenous medications, and parenteral nutrition, can be delivered on an outpatient basis. As a result, the nurse's role in educating the patient and family is an extremely important part of successful SCT; the patient and caregivers must be able to identify problems, such as fever or pulmonary and/or renal compromise (Buchsel & Whedon, 1995; Ezzone & Pokorny, 2007). Additionally, the nurse in a community health agency providing follow-up care after the patient's return home should learn the potential long-term complications and rehabilita-

tion concerns for the SCT patient (Buchsel & Whedon, 1995; Ezzone & Pokorny, 2007). Some points of education before, during, and after SCT include vascular access, dietary requirements, signs of infection, and psychosocial and financial resources. The patient, along with the caregiver and other members of the family support system, also must receive extensive education regarding post-transplant medications, general health guidelines, and follow-up requirements.

Even with the best nursing care, hematopoietic SCTs may not be successful because of disease recurrence or regimen-related toxicity. Although SCTs are used more widely today than previously, Copelan (2006) emphasized that SCTs are "broadly underused" and observed that socioeconomic factors continue to contribute to the decision of whether to seek transplantation; all too often, SCT is considered too late or not at all. Obviously, the potential benefit of transplantation must be balanced against the various risks, and the financial condition and health insurance benefits of the patient. Because the SCT affects the patient's family members, they must be included in transplant decisions earlier, rather than later, in the process. Clearly, the nurse who knows what the transplant process entails can help the patient and his or her loved ones manage the complexity of care and the associated risks with sound clinical knowledge, good communication, and attention to all aspects of the patient's well-being.

A special interest group solely dedicated to the concerns of bone marrow transplant nurses exists within the Oncology Nursing Society (ONS). Group members can be accessed for their expertise in caring for SCT patients before and after treatment and into survivorship through ONS (<http://www.ons.org/>). Additionally, an excellent text with detailed, understandable information about SCT was recently

published by Jones and Bartlett (Ezzone & Pokorny, 2007) and is included in the reference list. ■

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Suggested Readings

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Objectives

This continuing nursing educational (CNE) activity is designed for nurses and other health care professionals who care for and educate patients and their families undergoing, or who have undergone, stem cell transplant for treatment of cancer. For those wishing to obtain CNE credit, an evaluation follows. After studying the information presented in this article, the nurse will be able to:

1. Review the process of stem cell transplantation (SCT).
2. Define autologous versus allogeneic SCT.
3. Discuss the transplant process.
4. Describe the nurse's role in SCT.

Answer Form:

1. If you applied what you have learned from this activity into your practice, what would be different?

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Evaluation	Strongly disagree			Strongly agree		
2. By completing this activity, I was able to meet the following objectives:						
a. Review the process of stem cell transplantation (STC).	1	2	3	4	5	
b. Define autologous versus allogeneic SCT.	1	2	3	4	5	
c. Discuss the transplant process.	1	2	3	4	5	
d. Describe the nurse's role in SCT.	1	2	3	4	5	
3. The content was current and relevant.	1	2	3	4	5	
4. The objectives could be achieved using the content provided.	1	2	3	4	5	
5. This was an effective method to learn this content.	1	2	3	4	5	
6. I am more confident in my abilities since completing this material.	1	2	3	4	5	
7. The material was (check one) ___new ___review for me						
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Comments
