Article

Autologous Hematopoietic Stem Cell Transplantation for Patients With Multiple Myeloma:
An Overview for Nurses in Community Practice

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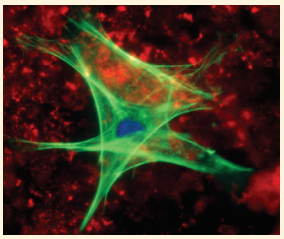

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Autologous hematopoietic stem cell transplantation (AHSCT) is approved for the treatment of select solid tumors, autoimmune disorders, and most hematologic malignancies. Multiple myeloma (MM) is the most common indication for AHSCT. Despite improvement in response and survival rates in the era of novel agents, AHSCT remains an important treatment option for patients with MM who are eligible. Clinical management of patients with MM requires a multidisciplinary approach that incorporates healthcare professionals in a number of clinical settings as well as caregivers and the patient. Patients about to undergo AHSCT are generally referred to tertiary care centers that specialize in ASCT. Pre- and post-transplantation treatments and long-term follow-up often are managed by a community-based referring oncologist in collaboration with the transplantation team. Oncology nurses play an integral role in the care of patients with MM in each clinical setting. This article aims to provide non-transplantation oncology nurses with guidelines for education, clinical management, and support of patients with MM undergoing AHSCT with a primary focus on the pre- and post-transplantation period.

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Hematopoietic stem cell transplantation (HSCT) is an accepted treatment for selected autoimmune and nonmalignant disorders, solid tumors, and hematologic malignancies. High-dose chemotherapy (HDC) is used in these settings to provide intensive cytotoxic therapy with the goal of eliminating malignant cells. However, the toxic effects of treatment are not specific to malignant cells alone, but affect all fast-growing cells. This results in expected side effects, most significantly bone marrow ablation (Antin & Yolin Raley, 2009). As such, reconstitution of the bone marrow and hematopoietic function using either autologous (patient's own) or allogeneic (related or unrelated donor) stem cells is integral to the treatment process. In both procedures, stem cells are collected prior to receiving HDC, processed, stored, and then infused into the patient following HDC. Without stem cell "rescue" following HDC, patients would not recover bone marrow function, causing significant risk of mortality from life-threatening infection, bleeding, or anemia (Antin & Yolin Raley, 2009; Bensinger, 2009; Kumar, 2009; Rodriguez, 2010b). The general process for HSCT is found in Figures 1 and 2 and further discussed in Faiman, Miceli, Noonan, and Lilleby (2013), published on pages 33–41 of this supplement.

Multiple Myeloma Overview

Multiple myeloma (MM) is a malignant plasma cell disorder. Plasma cells produce immunoglobulin, which are proteins critical to the protective immune response. Immunoglobulins consist of a heavy chain (IgG, IgA, IgM, IgD, IgE) and a light chain (kappa or lambda) (Mangan, 2010). In MM, atypical plasma cells produce excess quantities of one of these proteins, referred to as paraproteins, monoclonal proteins, or M proteins. The patient-specific myeloma subtype is categorized by the involved immunoglobulin (heavy chain and light chain) (e.g., IgG kappa). Several factors are thought to play a role in the malignant transformation of plasma cells, including chromosome changes, molecular characteristics, and elements that affect the bone marrow microenvironment such as cytokine abnormalities. Many of these factors are thought to have prognostic significance (Palumbo & Anderson, 2011).

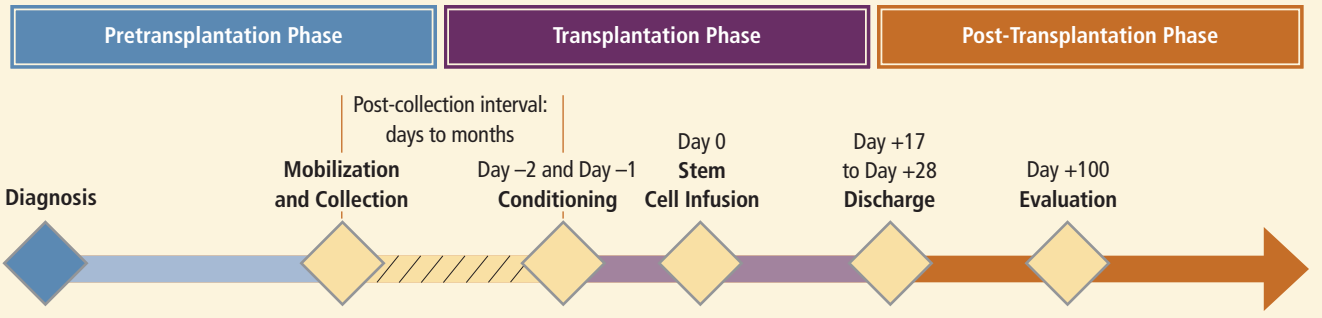
The diagnosis of MM is based on the presence of greater than 10% atypical plasma cells in the bone marrow, presence of a monoclonal protein in the peripheral blood and/or urine, and additional laboratory and clinical findings (Durie et al., 2006; Kyle et al., 2003). The common clinical manifestations of MM are the byproduct of excess paraprotein and its impact on the cellular environment and organs, and include anemia, fatigue, hypercalcemia, bone disease, bone pain, renal dysfunction, and decreased immune function (Kyle et al., 2003; Mangan, 2010).

Autologous Versus Allogeneic Hematopoietic Stem Cell Transplantation

MM is the second most common hematologic malignancy, but is the most common indication for autologous HSCT (AHSCT) (Pasquini & Wang, 2011). Multiple studies demonstrate a survival benefit associated with AHSCT; therefore, AHSCT is considered the standard of care for eligible patients (Attal, 1996; Giralt et al., 2009; Kumar, 2009). Allogeneic HSCT (allo-HSCT) differs from AHSCT in that marrow created by donor cells can promote new immune activity in the recipient, providing a graft-versus-host disease (or antimyeloma) effect. Allo-HSCT is associated with high treatment-related morbidity and mortality and should only be pursued in the setting of a clinical trial (Bensinger, 2009; Lokhorst et al., 2010). Therefore, the focus of these guidelines will be directed toward AHSCT.

Treatment From Induction to Post-Transplantation Recovery

When designing the plan of care for a patient with MM, all treatment options should be considered. Every newly diagnosed patient with MM, even those older than age 70 years, should be considered a candidate for an AHSCT. Eligibility criteria vary by institution. Referral to a transplantation center, most often based on proximity and insurance contracting, should be made early in the treatment process when considering AHSCT (National Comprehensive Cancer Network [NCCN], 2013; Palumbo et al., 2011). More than 150 medical institutions



Pretransplantation phase: Weeks to months prior to transplantation. Community providers are responsible for care.

Transplantation phase: Up to eight weeks. AHSC harvesting may be included or independent of transplantation phase. Transplantation center is responsible for care.

Post-Transplantation phase: Ongoing following discharge. Community providers are responsible for care. Day +100 evaluation takes place at the transplantation center.

AHSCT—autologous hematopoietic stem cell transplantation

FIGURE 1. Phrases and Terminology of Transplantation

Note. Based on information from Antin & Yolin Raley, 2009; Buschell & Kapustay, 2009; Kumar, 2009; Tariman, 2010.

- **Collection:** Apheresis is a procedure allowing for CD34-positive cell selection and can take 4–6 hours. The number of sessions is variable depending on the overall goal of collection and daily stem cell yield. Time ranges from 1–10 days. Once collected, the cells are cryopreserved in a medium of DMSO to prevent cell breakdown and may be stored for an indefinite period of time.
- **Collection Goal:** A minimum of two million CD34-positive cells (2×10^6 CD34-positive cells per kg of recipient weight) is generally accepted, but higher yields can result in more rapid bone marrow recovery following HDC. With the availability of plerixafor, stem cell harvesting has become more predictable and mobilization failure is less frequent. Plerixafor has been shown to improve cell yield, reduce number of apheresis sessions, and provide timely engraftment following HDC. The number of transplantations planned is physician- and patient-dependent; therefore, the goal is variable.
- **Conditioning:** The preparative regimen used to treat the underlying disease prior to AHSCT is referred to as conditioning. In multiple myeloma, melphalan is the chemotherapy agent of choice and is given as an IV infusion. The standard dose is 200 mg/m^2, but dose reductions may be made for impaired renal function, advanced age, or comorbid conditions.
- **Engraftment:** Blood count recovery, or engraftment, may be seen as early as 10 days following AHSC infusion. Engraftment is established when absolute neutrophils are greater than 500 cells per dl for three consecutive days, or greater than 1,000 cells per dl for one day, and platelets remain greater than 20,000 mm^3 independent of transfusion for at least seven days.
- **Mobilization:** Stimulation and movement of AHSC from the bone marrow into the peripheral blood is known as mobilization. Methods include using G-CSF as a single agent, with or without chemotherapy or with or without plerixafor. This may take 1–2 weeks depending on the approach. Venous access is necessary for apheresis, either via peripheral veins, if access is sufficient, or the placement of a dialysis-like central venous catheter may be required.
- **Stem Cell Infusion:** The day of infusion, or transplantation, is commonly referred to as day 0. The previously cryopreserved AHSCs are thawed and infused via central venous access. The actual infusion can take as long as an hour depending on the number of frozen bags of AHSC product. There may be other activities as part of the infusion (i.e., hydration) that will result in a day-long procedure. The patient will have a distinctive odor after the infusion from the DMSO preservative.
- **Transplantation Side-Effect Management:** Anticipated side effects from the HDC include alopecia, gastrointestinal toxicity (nausea, vomiting, diarrhea, anorexia, mucositis), and bone marrow ablation (pancytopenia). Antiemetics, hydration, pain management, antibiotics, and transfusion support are necessary during the acute post-transplantation phase.

AHSCT—autologous hematopoietic stem cell transplantation; DMSO—dimethyl sulfoxide; G-CSF—granulocyte–colony-stimulating factor; HDC—high-dose chemotherapy

FIGURE 2. Terminology of the Mobilization, Collection, and Transplantation Processes

Note. Based on information from Antin & Yolin Raley, 2009; Buschell & Kapustay, 2009; DiPersio, Stadtmauer, et al., 2009; DiPersio, Uy, et al., 2009; Gertz et al., 2009; Giralt et al., 2009; Tariman, 2010.

exist in the United States that perform AHSCT (Blood and Marrow Transplant Information Network, 2013; Center for International Blood and Marrow Transplantation, 2013). Each institution has specific protocols for pretransplantation screening, evaluation, consultation, and treatment planning. Transplantation eligibility is largely based on age, performance status, and desire to undergo the procedure (see Figure 3). The screening and approval process may take weeks to months. Ultimately, transplantation eligibility should be determined by a transplantation specialist.

Once a patient is diagnosed with active MM, the patient will initiate a treatment plan that includes chemotherapy. The goal is to effectively suppress the malignant clone and optimally reach a complete response prior to the collection of stem cells. Patients with MM who are eligible for transplantation should not receive regimens containing melphalan prior to stem cell collection because it can interfere with stem cell mobilization (Cavo et al., 2011; Giralt et al., 2009). Novel therapies (thalidomide, lenalidomide, pomalidomide, bortezomib, and carfilzomib), in combination with dexamethasone or standard chemotherapeutic agents, have demonstrated improved response rates (RR) and overall survival (OS) in patients with MM and are considered acceptable regimens prior to HSCT (Cavallo et al., 2011; Kyle & Rajkumar, 2009; Lacy et al., 2012; NCCN, 2013; Sonneveld, Asselbergs, et al., 2012). For those patients deemed transplantation ineligible, melphalan and other alkylating agents in combination with novel agents have shown significant responses and improved OS (Palumbo et al., 2011; Rajkumar et al., 2010; San Miguel et al., 2008). A number of clinical trials that include initial therapy, supportive care, maintenance, or treatment of relapse in the clinical trial setting currently are being conducted. Participation in clinical trials should be considered at all phases of treatment when possible.

AHSC collection and transplantation is a multistep process. The timing for stem cell collection is individualized based on the transplantation plan. For example, a patient may collect stem cells for storage purposes and continue with current therapy, or collect stem cells with the intent to proceed directly to AHSCT. Patients who previously collected and stored stem cells will proceed with HDC and AHSCT when clinically indicated without repeating the collection process. Certain side effects and clinical implications are common to therapies used at each stage of the process (see Table 1). Preparing for all phases of the transplantation process can be overwhelming for patients. Figure 4 and Appendix A provide considerations and Internet resources that may assist patients and caregivers.

Post-Transplantation Recovery

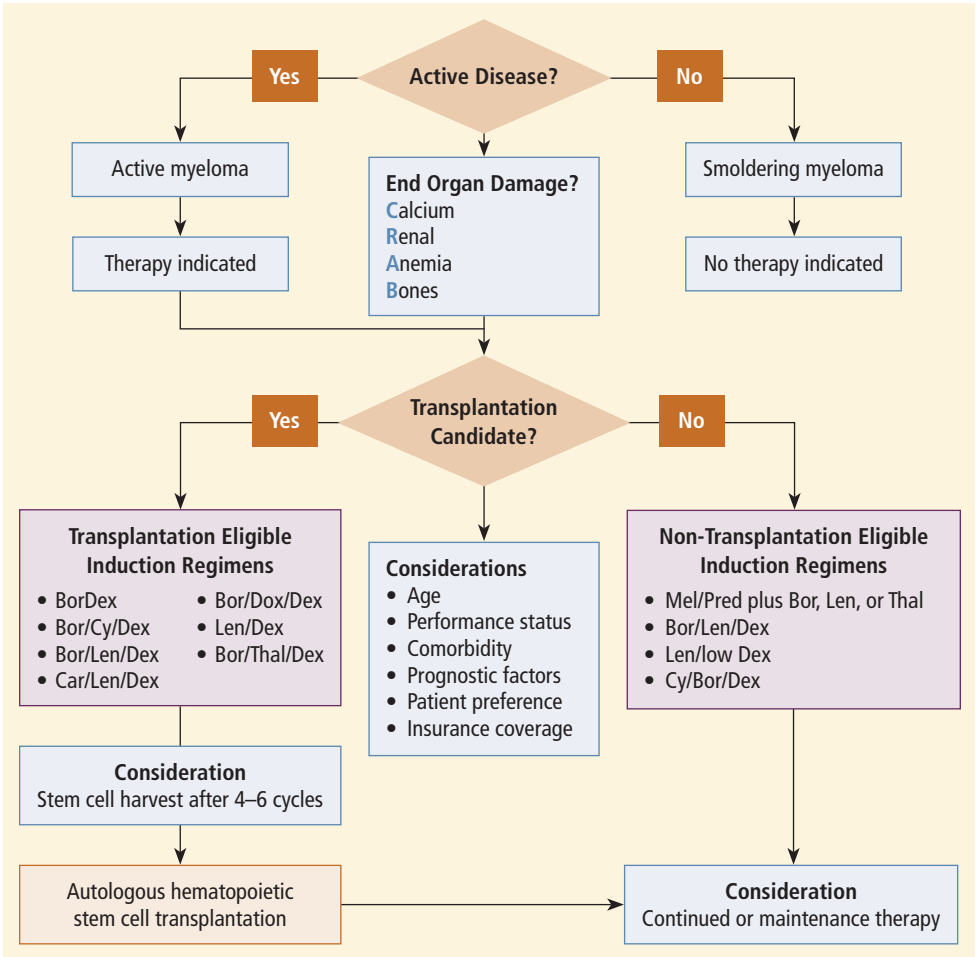
The post-transplantation period begins after recovery from acute toxicity of the HDC, including blood count recovery (Kelley, McBride, Randolph, & Leum, 2000; Williams, 2004). This period of time has become obscured because of the many discharge options and individualized practices at each transplantation center. Patient acuity at time of discharge is higher than in years past, and the care of the patient with MM who has

received AHSCT often is complex (Bevans, 2009). The majority of post-transplantation care becomes the responsibility of non-transplantation practitioners and caregivers. Patients anticipate the return home from the transplantation center, but also may experience anxiety in the transition.

The International Myeloma Foundation Nurse Leadership Board has compiled a summary of guidelines, recommendations, and clinical management strategies intended to optimize the quality of life (QOL) of patients undergoing transplantation and to minimize adverse events during the immediate post-transplantation period. The goal is to assist the community-based healthcare team, including oncology healthcare providers, to ease the transition from transplantation center to community, relieve anxieties, and provide information to guide the recovery of the patient after AHSCT. While reviewing these guidelines, note that QOL may improve over time. In several studies, transplantation-related symptoms and QOL improved or surpassed the pretransplantation level when measured at 6–12 months (Chao et al., 1992; Lyons et al., 2011; McQuellon et al., 1998; Saleh & Brockopp, 2001; Schulmeister, Quiett, & Mayer, 2005).

Considerations for the Nontransplantation Oncology Nurse

Discharge guidelines vary among transplantation centers, but generally include suggested management of psychological and physical needs of the patient. Although patients and their caregivers receive extensive education verbally and in writing prior to their discharge from the transplantation center, the amount of information may be overwhelming, and specific details forgotten. Therefore, ongoing educational reinforcement is essential for both patients and their caregivers. Familiarity with the discharge procedures and post-transplantation policies at the particular transplantation center from which the patient has been discharged will allow for reinforcement of key concepts when healthcare providers meet with patients and their families. If not provided to the patient at discharge, written instructions can be requested from the transplantation center to help guide care. Long-term survivorship issues also should be considered when caring for the patients with MM post-transplantation. Guidelines addressing fertility, sexuality, renal aspects, bone health, health maintenance, and mobility and safety can be found in a previous supplement to the *Clinical Journal of Oncology Nursing* from the International Myeloma Foundation Nurse Leadership Board (Bilotti et al., 2011; Bilotti, Gleason, & McNeill, 2011; Faiman, Mangan, Spong, & Tariman, 2011; Miceli, Colson, Faiman, Miller, & Tariman, 2011; Richards, Bertolotti, Doss, & McCullagh, 2011; Rome, Jenkins, & Lilleby, 2011).



Bor—bortezomib; Car—carfilzomib; Cy—cyclophosphamide; Dex—dexamethasone; Dox—doxorubicin; Len—lenalidomide; Mel—melphalan; Pred—prednisone; Thal—thalidomide

FIGURE 3. Treatment Algorithm for Newly Diagnosed Multiple Myeloma

Note. Based on information from Mikhael et al., 2013; National Comprehensive Cancer Network, 2013.

Post-Transplantation Needs

The psychological impact of AHSCT should not be overlooked. Patients often describe the "let down" feeling after working hard before and during the transplantation, and many reflect on the events leading up to the transplantation and the details of the transplantation after being discharged. Transplantation recovery can be associated with physical setbacks as well as social strain on the caregiver and family. In fact, post-transplantation psychological issues may present greater challenges than the medical needs of the patient for the community-based healthcare team (Cooke, Gemmill, Kravits, & Grant, 2009).

The estimated rate of depression following stem cell transplantation ranges from 25%–50%. Depression affects physical health, can increase symptom-related

distress, decrease survival, and has been associated with a higher incidence of suicide. Early identification of the symptoms of depression will allow the post-transplantation healthcare team to intervene early and refer the patient for more intensive services, such as psychiatric or social services and referral back to the transplantation center. In some cases, antidepressive medications may be necessary. Caregivers and family members should be made aware of the frequency of post-transplantation depression, signs and symptoms they should report, and how best to contact the appropriate healthcare provider (Cooke et al., 2009).

Post-Transplantation Symptom Management

Symptom management is vital for patients after stem cell transplantation. Persistent symptoms of HDC-related toxicity are common even after the patient has returned home (see Table 2).

TABLE 1. Common Multiple Myeloma Therapies, Side Effects, and Clinical Implications

Drug, Class, Route	Potential Side Effects and Toxicities	Clinical Implication	Additional Information[a]
Myeloma Therapy Medications			
Bortezomib Proteasome inhibitor IV or SQ administration	MS, PN, diarrhea or constipation, irritation or erythema at injection site; VZV activation	Monitor CBC, monitor PN symptoms, bowel management; use antiviral prophylaxis	Used as combination therapy or single agent; consider SQ administration to reduce PN
Carfilzomib Proteasome inhibitor IV administration	Fatigue, anemia, thrombocytopenia, nausea, diarrhea, dyspnea, and fever	Monitor CBC and liver function tests. Prevent tumor lysis syndrome via PO and IV hydration; premedicate with dexamethasone in the first cycle	Approved for patients who have had two or more prior therapies, including bortezomib and an immunomodulatory agent
Lenalidomide Immunomodulator Oral administration	MS, thromboembolic event when combined with steroids, and skin rash	Monitor CBC, bowel management, dose adjust for renal impairment; thromboembolic event prophylaxis	Used as combination therapy or as single-agent maintenance; hold for two weeks prior to autologous hematopoietic stem cell collection
Melphalan Alkylator IV or oral administration	For conventional doses, MS; for high doses, myeloablation, GI disturbance, and alopecia	Monitor CBC	Should be avoided prior to autologous hematopoietic stem cell collection; long-term use can cause myelodysplasia
Pomalidomide Immunomodulator Oral administration	MS and thromboembolic event	Monitor CBC, bowel management; thromboembolic event prophylaxis	Approved for patients who have had two or more prior therapies, including bortezomib and an immunomodulatory agent
Thalidomide Immunomodulator Oral administration	MS, thromboembolic event when combined with steroids, PN, and constipation	Monitor CBC, bowel management; thromboembolic event prophylaxis	Used in combination with dexamethasone
Supportive Care Medications			
G-CSF/filgrastim Cytokine SQ administration	Joint and bone pain; increased white blood cells	Assess and medicate for pain.	Management of neutropenia; autologous hematopoietic stem cell mobilization
Pamidronate Bisphosphonate IV administration	Initial phase reaction, hyperalbuminuria, and osteonecrosis of the jaw	Dental evaluation prior to start (if possible), regular dental cleaning; avoid invasive dental procedure while receiving treatment	Inhibition of bone resorption and associated hypercalcemia. See ASCO and IMWG guidelines for duration of use. May be held during transplantation and resumed after.
Plerixafor Chemokine inhibitor SQ administration	Diarrhea and erythema at injection site	Bowel management	Used in combination with G-CSF for stem cell mobilization
Zoledronic acid Bisphosphonate IV administration	Initial phase reaction, hyperalbuminuria, and osteonecrosis of the jaw	Dental evaluation prior to start (if possible), regular dental cleaning; avoid invasive dental procedure while receiving treatment	Inhibition of bone resorption and associated hypercalcemia. See ASCO and IMWG guidelines for duration of use. May be held during transplantation and resumed after.

[a] See package insert for a complete listing of possible side effects. Practical use of medications may differ from U.S. Food and Drug Administration-approved indications and is done at the discretion of a licensed provider.

ASCO—American Society of Clinical Oncology; CBC—complete blood count; G-CSF—granulocyte–colony-stimulating factor; GI—gastrointestinal; IMWG—International Myeloma Working Group; MS—myelosuppression; PN—peripheral neuropathy; SQ—subcutaneous; VZV—varicella zoster virus

Note. Based on information from Amgen Inc., 2013; Bertolotti et al., 2008; Bilotti, Gleason, et al., 2011; Bristol-Myers Squibb, 2005; Celgene Corporation, 2013a, 2013b, 2013c; Genzyme: A Sanofi Company, 2010; GlaxoSmithKline, 2008; Kumar, 2009; Millennium: The Takeda Oncology Company, 2012; Novartis Pharmaceuticals, 2012a, 2012b; Onyx Pharmaceuticals, 2012.

Post-Transplantation Infection Risk and Prevention

Post-transplantation infection is a major cause of morbidity and mortality. Although the patient's white blood cell count and absolute neutrophil count may be within the normal range, the cells are functionally abnormal, placing the patient at increased risk for infection. In addition, continued physical weakness and malnutrition make recovery from a new infection difficult. Therefore, prophylactic antibiotics to prevent post-transplantation infections, such as invasive pneumococcal infection and pneumocystis pneumonia, are recommended for as long as one year following AHSCT (Tomblyn et al., 2009). Early detection and prompt intervention for infection is essential in caring for patients with MM (Palumbo et al., 2012). Careful assessment of the skin, lungs, gastrointestinal, renal, and skeletal systems are needed in identifying infection. Vital signs should be monitored at each clinic visit and patients should monitor their own vital signs as instructed by their care provider. Potential post-transplantation infections and preventions are listed in Table 3.

Frequent and meticulous hand washing by the patients and those they come in contact with is very important to prevent the transfer of infection. Many transplantation centers recommend that patients wear a mask when coming into a clinic or hospital for appointments. Patients may be advised to avoid public places such as restaurants, movies, or shopping malls. The suspension of these precautions will vary by individual centers and should be discussed in detail with the transplantation center.

- **American Cancer Society**
  Information on disease types and available support
  www.cancer.org
- **Be the Match: National Marrow Donor Program**
  Transplantation-related information for patients and caregivers
  www.marrow.org
- **BMT Information Network**
  Transplantation-related information for patients and caregivers
  www.BMTInfoNet.org
- **Caring Bridge**
  A site to create a personal blog or journal that can be shared with family and friends
  www.caringbridge.org
- **International Myeloma Foundation**
  Information about myeloma, research, and available support
  www.myeloma.org
- **Leukemia and Lymphoma Society**
  Information on disease types and available support
  www.lls.org
- **Multiple Myeloma Research Foundation**
  Information about myeloma, research and available support
  www.themmrf.org
- **National Bone Marrow Transplant Link**
  Transplantation-related information for patients and caregivers
  www.nbmtlink.org
- **National Cancer Institute**
  Information on disease types and research
  www.cancer.gov

Note. Website addresses and content can change; therefore, the information should be reviewed before sharing with patients.

FIGURE 4. Web Resources

Implications for Practice

- Include healthcare professionals from a number of clinical settings to best address the multidisciplinary approach required to manage multiple myeloma.
- Become familiar with the autologous hematopoietic stem cell transplantation process, as it remains an important treatment option for multiple myeloma.
- Incorporate guidelines for post-transplantation management in the community setting to promote quality of life and improve survival for patients.

Recommendations concerning personal hygiene, home maintenance, and cleanliness also may be provided by the transplantation center to further reduce the risk of infection. Guidelines for laundering clothes and housekeeping, particularly facilities used by the patient, are commonly provided. Specific policies regarding personal hygiene also are often recommended. It must be kept in mind that the patient may not be able to perform some of these duties independently in the first months following HSCT, emphasizing the need to include caregivers in the education process (Antin & Yolin Raley, 2009). The role of caregivers in the recovery of patients with HSCT is discussed in greater detail by Kurtin, Lilleby, and Spong (2013) on pages 25–32 of this supplement.

Because of the risk of food-borne infection, specific nutritional and dietary guidelines may be mandated by the transplantation center. Nutritional recommendations and restrictions may begin at the start of HDC and continue after discharge. In general, the Advisory Committee on Immune Practices recommends foods that have been refrigerated, pasteurized, or well-cooked for patients during the post-transplantation period (Antin & Yolin Raley, 2009; Tomblyn et al., 2009).

Smoking tobacco is prohibited after an AHSCT for many reasons. People who smoke are at increased risk for developing pneumonia as well as pulmonary and cardiovascular toxicity related to AHSCT. Marijuana use is prohibited because of the heightened risk of fungal infection associated with inhalation. Alcohol consumption also is restricted because of its potential effect on the liver, platelets, and immune function (Sipsas & Kontoyiannis, 2008; Tichelli et al., 2008; Versteeg, Slot, van der Velden, & van der Weijden, 2008).

Post-Transplantation Immunizations

The transplantation process results in a loss of T and B lymphocytes which, in turn, causes loss of immune memory. Immune memory is shaped by the culmination of exposure to infectious agents, environmental antigens, and vaccines during a person's lifetime (Kroger, Sumaya, Pickering, & Atkinson, 2011; Stadtmauer et al., 2011). Therefore, patients require reimmunization.

Post-transplantation immunizations vary by institution. Based on the Centers for Disease Control and Prevention and Advisory Committee on Immune Practices recommendations, non-live vaccines may be administered as early as three months post-transplantation. Live-attenuated vaccines may be administered two years following transplantation in immune-competent people (Tomblyn et al., 2009). An example of an immunization schedule can be found in Table 4.

TABLE 2. Post-Transplantation Symptoms, Clinical Findings, and Management Strategies

Symptom	Clinical Findings and Risk Factors	Management Strategies
Anorexia	Weight loss, taste changes, change in performance status, fatigue, nausea and vomiting, and diarrhea	Review medications for possible source. Medical nutritional therapies: oral nutritional supplements, IV hydration Small frequent meals, calorie counts, weekly weight, nutritional consult Reinforce improvement with time. Adjust medications as needed. Treat underlying cause (e.g., medication for nausea and vomiting).
Anxiety and depression	Fatigue, exhaustion, difficulty sleeping, difficulty concentrating, restlessness, irritability and impatience, recurrent thoughts of diagnosis and treatment, and anorexia	Listen to and validate concerns. Referral to social services, psychiatry, and support groups Pharmacologic: anti-anxiety medication, antidepressants Complementary and alternative medicine therapy: relaxation therapy, mild exercise such as walking
Diarrhea	Increased frequency of bowel movements, abdominal cramps, dehydration, and decrease in weight	Review medications for possible source (i.e., antibiotics, narcotic withdrawal). Electrolyte evaluation Stool sample for enteric pathogens (i.e. *Clostridium difficile*) Anti-diarrheal medication Appropriate fluid and electrolyte replacement Adjust diet for food sensitivities: milk products, certain spicy foods, nutritional supplements, fatty foods, chocolate Antibiotics as needed; adjust medications as needed
Fatigue	Decrease in energy, inability to complete tasks, insomnia or hypersomnia, not feeling rested after sleeping at night, and generalized weakness	Review medications that may cause fatigue. Assess for anemia. Mild exercise such as walking Potentially decrease or discontinue medications that cause fatigue. Counsel patient on sleep hygiene, such as minimizing napping or staying in bed throughout the day. Erythropoietin medication if indicated and after obtaining written consent Red blood cell transfusion, if needed
Fever	Diarrhea, muscle weakness, fatigue, confusion, and seizures	Panculture, chest x-ray, and CBC with differential and platelets Prophylactic antibiotics if neutropenic; therapeutic antibiotics if culture positive Acetaminophen, IV hydration, symptom management Monitor for fever greater than 101.3°F (and lower temperatures if patients are not feeling well), blood pressure declining from baseline and tachycardia
Nausea and vomiting	Anorexia, nausea and vomiting, weight loss, and diminished skin turgor	Quantify episodes of emesis. Assess fluid and electrolyte status. Review medications for antiemetics and medications that may cause nausea and vomiting. Adjust medications if possible and as needed. IV or oral hydration and replace electrolytes as needed
Pain	Assess for new or existing pain symptoms, current pain medication, assess for pain related to infection, and assess for symptoms of depression or anxiety	Appropriate pain medication regimen: long-acting pain medication together with breakthrough pain medication, doses titrated to effectiveness Consider imaging for source of new or worsening pain Consult with appropriate specialty, if indicated
PN	Paresthesias, impaired proprioception, pain, and sensory deficits; patients at increased risk: those with a history of diabetes, alcohol use, vitamin B_{12} deficiency, paraneoplastic syndrome, and vascular insufficiency	Baseline assessment of PN, description of PN symptoms, previous chemotherapy, current medications, neurologic examination including sensory and motor use Safety evaluation and nutritional assessment Treatment of neuropathic pain: medications, acupuncture, massage, medications Promote safety with use of assistive devices: cane, orthotics, wheelchair. Physical therapy and activity; massage
Thrombosis (DVT or PE)	Painful, swollen and erythematous extremity (most often lower extremity), shortness of breath, tachycardia, chest pain, and HTN; patients at increased risk: those with obesity, diabetes, cardiovascular disease, HTN, hyperlipidemia, immunomodulatory agents with concurrent high-dose steroids, anthracyclines, ESAs, hospitalizations, and immobility	Prevention: thromboprophylaxis for all patients at risk Full therapeutic anticoagulation for any patients with more than two risk factors If DVT or PE is suspected: Doppler ultrasound of suspected extremity High-resolution chest CT with PE protocol if PE is suspected Medication to treat thrombosis: low molecular weight heparin, warfarin, and alternative anticoagulants Consult with coagulation specialist if appropriate.

CBC—complete blood count; CT—computed tomography; DVT—deep vein thrombosis; ESA—erythropoietin-stimulating agent; HTN—hypertension; PE—pulmonary embolus; PN—peripheral neuropathy

Note. Based on information from Antin & Yolin Raley, 2008; Eaton & Tipton, 2010; Rodriguez, 2010a.

Post-Transplantation Medication Considerations

Polypharmacy during transplantation is common and can be confusing. Therefore, many transplantation teams will provide patients and their families with a medication chart to help track and maintain the dose and the administration of scheduled and "as needed" medications. Pretransplantation and transplantation-specific medications are added, discontinued, and adjusted frequently according to the patient's needs during the acute care phase of the transplantation. Hypertension and hyperglycemic management regimens, in particular, often require modifications during the transplantation process. A list of discharge medications should be provided to the patient as well as to the discharge facility or homecare agency and the patient's referring oncologist involved in the patient's care. Patients may be restricted from taking certain over-the-counter medications such as nonsteroidal anti-inflammatory drugs and supplements because of drug interactions, organ toxicity, or interference with therapy. Medications must be taken as prescribed and medication changes should be discussed with the staff at the transplantation center.

Disease Management Following Autologous Hematopoietic Stem Cell Transplantation

Although AHSCT remains an important treatment strategy for patients with MM, relapse of MM is inevitable for the majority of patients. The timing is unpredictable and relapse can occur at any time following AHSCT, ranging from months to years. Those considered at high risk based on stage of disease and cytogenetics are at greater risk of early relapse (Mikhael et al., 2013; Palumbo & Cavallo, 2012). Providing patients with the clear message is important so that when progression does occur, they understand that it does not necessarily indicate end of life, but, rather, a time for change in therapy. Determining the optimal time to next therapy remains a controversial issue following AHSCT, and several studies are ongoing. Data

TABLE 3. Common Transplantation Infections and Prevention

Infection	Type of Infection	Prevention
Bordetella pertussis (whooping cough)	Community-acquired bacterial respiratory infection	If exposed, prevention and treatment available (azithromycin or SMX/TMP) If hospitalized, proper precautions should be taken to avoid transmitting to others. A cellular vaccine is recommended.
Community respiratory viruses: RSV, influenza, adenovirus, and parainfluenza	Viral infections that can progress to bronchitis or pneumonia RSV is more common in infants, but can be seen in older adults and ICHs. Influenza accounts for about 20% of respiratory viral infection in patients who receive a transplantation. Adenovirus may manifest as a diarrheal illness.	Handwashing; ICHs should wear a mask, clean hard surfaces with anti-infective wash, and avoid crowds and people with respiratory symptoms. If hospitalized, proper precautions should be taken to avoid transmitting to others. Antiviral medication may be available. Inactivated influenza vaccine should be administered to the patient and direct caregivers unless contraindicated. Do not use the live inhaled version. May begin as early as 3–6 months post-transplantation and every year of life.
Pneumocystis carinii pneumonia (renamed as PJP)	Protozoal infection that can develop in ICHs. ICHs and patients with AHSCT may develop PJP if prophylaxis is not provided; can occur early after transplantation, particularly if the patient has been heavily treated beforehand.	SMX/TMP, atovaquone, dapsone, or aerosolized pentamidine, depending on allergy profile Prophylaxis for 3–6 months following AHSCT
Streptococcus pneumonia or invasive pneumococcal infection	A gram-positive encapsulated organism that can cause sudden and serious systemic infection in patients following AHSCT. Considered a late transplantation complication and is common in patients with multiple myeloma because of decreased humoral immunity	Penicillin or doxycycline, depending on allergy profile Prophylaxis for 12 months following AHSCT, until revaccinated Pneumococcal vaccine should be administered as a 7-valent or 23-valent vaccine as early as 3–6 months post-transplantation.
Viridans streptococci	Organism found commonly in the oral cavity Greatest concern during times of oral mucositis	Quinolone therapy for neutropenic state longer than seven days.
VZV (shingles)	Primary infection, commonly known as chicken pox. VZV persists in the sensory nerve ganglia. Reactivation is common in older adults or ICHs.	Acyclovir or valacyclovir therapy for one year or while on active treatment Also prevents herpes simplex virus, type I and II The shingles vaccine is a live virus and currently not recommended for patients with multiple myeloma.

AHSCT—autologous hematopoietic stem cell transplantation; ICH—immunocompromised host; PJP—*Pneumocystis jiroveci* pneumonia; RSV—respiratory syncytial virus; SMX/TMP—sulfamethoxazole/trimethoprim; VZV—varicella zoster virus

Note. Schedule and use vary between transplantation centers.

Note. No live vaccines should be given in the first year following transplantation.

Note. Based on information from Antin & Yolin Raley, 2009; Centers for Disease Control and Prevention, 2012; Cordonnier et al., 2010; Stadtmauer et al., 2011; Tomblyn et al., 2009.

TABLE 4. Post-Transplantation Immunization Schedule

Organism	Vaccine	Time Post-HSCT to Initiate Vaccine	Dose and Route	Comments
Inactivated Vaccines				
Pneumococcal	PCV7/ PPSV23	3–6 months	0.5 ml IM or SQ	Can be given six months post-transplantation
Pertussis, tetanus, diptheria	DTAP	6–12 months	0.5 m. IM	Can be given six months post-transplantation
Haemophilus influenzae type B	HIB	6–12 months	0.5 ml IM	Can be given six months post-transplantation
Hepatitis B	–	6–12 months	1 ml IM	Administer to patients who are hepatitis B virus negative.
Meningococcus	–	6–12 months	0.5 ml SQ	Recommended in areas with an increase in meningococcus
Influenza	–	4–6 months	0.5 ml IM (the nasal version is live and, therefore, not recommended)	Give annually as available in the autumn months. May administer four months post-transplantation; however, two doses of the vaccine are suggested.
Live Virus Vaccines				
Measles, mumps, and rubella	MMR	24 months	0.5 ml SQ	MMR should not be given if the patient is immunosuppressed.
Varicella zoster virus (shingles)	Zoster vaccine	Not currently recommended. Clinical trials are ongoing.	–	Not currently recommended; inactivated version is under investigation. Prevention with antiviral medication is recommended.

HSCT—hematopoietic stem cell transplantation; IM—intramuscular; SQ—subcutaneous

Note. Based on information from Cordonnier et al., 2010; Kroger et al., 2011; Ljungman et al., 2009; Tomblyn et al., 2009.

regarding the use of maintenance therapy following HSCT for MM continue to be reported. Attal et al. (2012) reported improvement in progression-free survival (PFS) following AHSCT using lenalidomide as maintenance therapy but no increase in OS. McCarthy et al. (2012) also reported an increase in PFS as well as a longer OS. Bortezomib can be used as maintenance post-transplantation as well, and may be associated with improvement in PFS (Sonneveld, Schmidt-Wolf, et al., 2012).

Conclusion

Care of the patient following AHSCT is complex, however, expected side effects of HDC usually are manageable. Although consistent objectives and goals are in place for AHSCT recipients, care must be individualized based on pretransplantation treatment toxicities and transplantation-related side effects. Community oncology professionals play a critical role in the collaborative management of the patient with MM throughout the treatment continuum. Consistent communication among the patient, the referring center, and the transplantation center is vital to ensure all testing, insurance approval, and support services are in place prior to starting the transplantation process. Post-transplantation guidelines are not standardized, and recommendations for post-transplantation care vary between transplantation centers. These factors add to the challenge of caring for the transplantation patient in a community-based setting.

All providers should assist in supporting the patient and family members through the transplantation journey. Discharge is an exciting time for the patient, but also can be physically challenging and emotionally overwhelming. Community providers are instrumental in monitoring and managing post-transplantation concerns. Understanding the AHSCT rationale, process, and needs of the patient post-transplantation will improve the QOL for the patient undergoing transplantation and impact OS. Maintaining a collaborative management approach with consistent communication between the transplantation center and community healthcare provider team will improve overall outcomes for patients undergoing transplantation.

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At the Transplantation Center

Consider bringing these items to the transplantation center consultation

- Medical records (i.e., radiology on disc, laboratory results, bone marrow reports)
- List of previous chemotherapy and dates received
- Current and recently taken medications (both prescribed and supplements)
- Questions for the physician

Important paperwork to bring

Medical Leave of Absence (MLOA), Family Medical Leave Act (FMLA), and insurance benefits. Notify your employer of MLOA and complete FMLA forms. Forms need to be completed for patient and caregivers. Anticipated time for processing is eight weeks.

Suggested items to bring for your stay

Comfortable clothing, sedentary activities, multi-unit pill dispenser, personal items of comfort, and cell phone

In the Community

While away from home . . .

- Arrange for caregiver support while at the transplantation center. Caregivers may be rotated. Investigate housing options near the transplantation center.
- Arrange for child and pet care.
- Arrange for care of your home while you are away and assistance when you return after transplantation (i.e., yard maintenance, mail delivery, and utilities).

Seek help with household chores and activities of daily living

- Assistance with cleaning, paying bills, grocery shopping, laundry
- Assistance with bathing, dressing, meal preparation, and transportation (medical appointments, shopping, pharmacy)
- Encouragement regarding oral intake, ambulation, and strengthening

Fundraising

Out-of-pocket expenses add up quickly. Consider hosting a fundraising event in your community to help cover healthcare costs.

Follow-Up Care

Long-term follow-up plan of action

Plan to return to the transplantation center near day 100 post-transplantation for a full evaluation. This may be a 2–3 day visit. Post-transplantation immunization may be recommended at 12, 14, and 24 months following transplantation.

Oral medication management

Administering scheduled and as needed medications, refills, and renewals

IV fluids and medications

In some situations, home infusion of medications for specific conditions (i.e., dehydration, infection, low magnesium) may be ordered by the healthcare provider.

Symptom monitoring

Fever, bruising, bleeding, new onset of pain (bone or nerve); changes in energy, appetite, weight (up or down), bowel function, and bladder function. Know your contact information—who to call, where to go.

Patient advocate

Communicate with healthcare providers, employers, family and friends; consider creating a blog to keep friends and family informed

Central line care

This varies from institution to institution. Instructions will be provided by the transplantation center.

APPENDIX A. Preparation and Activity Considerations for Patients With Multiple Myeloma Undergoing Hematopoietic Stem Cell Transplantation