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Hematologic Effects

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This excerpt, chapter 7 from the book *Hematopoietic Stem Cell Transplantation: A Manual for Nursing Practice,* edited by Susan A. Ezzone, MS, RN, CNP, is part of a series of clinically relevant reprints that appear regularly in the *Clinical Journal of Oncology Nursing.*

The most common hematologic effects post-transplant include neutropenia, immunosuppression, thrombocytopenia, anemia, graft failure, and delayed engraftment. Although the most common cause of the complications is the transplant preparative regimen, other etiologic risk factors may occur. This chapter will discuss the pathophysiology, etiology, and management of each hematologic complication.

Neutropenia

Neutropenia and associated infections following transplant are the most common complications of hematopoietic stem cell transplant (HSCT). Many steps have been made toward limiting transplant-associated neutropenia and infections; however, infection remains the leading cause of post-transplant mortality and morbidity (Nichols & Boeckh, 2000). In addition, this complication has been found to add significant costs to the transplant procedure. In autologous transplantation, infection may add approximately $18,400, and for allogeneic transplantations, approximately $15,300 may be added to the cost of the procedure during the first 100 days post-transplant (Lee, Klar, Weeks, & Antin, 2000).

In caring for transplant recipients, it is vitally important to understand the neutropenic process and the diagnosis and treatment of infections often associated with neutropenia. The immune system of the transplant recipient is severely insulted by high-dose chemotherapy, with or without radiation, given prior to the transplant. Prolonged periods of neutropenia, combined with other complications of transplant, including impaired skin and mucosal integrity, graft versus host disease (GVHD), graft rejection, steroid therapy, malnutrition, and invasive venous catheters, increase HSCT recipients' risk for morbidity and mortality related to severe infections (Ellerhorst-Ryan, 1997; Walker & Burcat, 1997).

Infection Risk in Neutropenic Patients

The body has two basic lines of defense against invasion of infection-causing pathogens. The first line is the skin and mucosal linings, and the second is the white blood cell (WBC). The WBC community contains granulocytes, monocytes, macrophages, and lymphocytes. Neutrophils that seek out and kill microorganisms that enter the body comprise approximately 95% of the granulocyte population, making them a prominent component for an adequate immune system (Alcoser & Burchett, 1999). Chemotherapy and/or radiation therapies decrease the number of these infection-fighting cells, resulting in a condition known as neutropenia. See Table 7-1 for the National Cancer Institute's Common Toxicity Criteria (version 2.0) grading system for neutropenia for HSCT. Profound neutropenia with an absolute neutrophil count (ANC) < 100 cells per microliter is common to the HSCT population as a complication resulting from high-dose chemotherapy and/or radiation therapy (Phillips, 1999).

The point at which the neutrophil count is maintained at > 500/mm³ is considered neutrophil engraftment (Centers for Disease Control and Prevention [CDC], Infectious Diseases Society of America, and American Society of Blood and Marrow Transplantation, 2000). The duration of neutropenia for the HSCT recipient depends on several factors, including history of chemotherapy and radiation therapy, the type and number of cells used for the transplant, preparative regimen used, the use of growth factors post-transplant, and post-transplant complications.

Neutrophil Engraftment

Two of the most recognized and important factors in the fight against early infectious complications post-transplant are the use of colony-stimulating factors and mobilized peripheral blood progenitor cells. Transplants utilizing peripheral blood progenitor cells that have been mobilized with hematopoietic growth factors (specifically granulocyte–colony-stimulating factor [G-CSF]) improve hematologic recovery post-transplant for both autologous and allogeneic HSCT (Beyer et al., 1995;

Table 7-1. Grading of Neutropenia Using the National Cancer Institute's Common Toxicity Criteria

SUBJECT	GRADE			
	1	2	3	4
Neutrophils/granulocytes (absolute neutrophil count/absolute granulocyte count) for BMT studies	$1.0 - < 1.5 \times 10^9/l$ $1,000 - < 1,500/mm^3$	$0.5 - < 1.0 \times 10^9/l$ $500 - < 1,000/mm^3$	$0.5 - < 0.5 \times 10^9/l$ $100 - < 500/mm^3$	$< 0.1 \times 10^9/l$ $< 100/mm^3$

Note. Based on information from the National Cancer Institute, 1999.

Pavletic et al., 1997). In the autologous transplant population, using mobilized peripheral blood stem cells (PBSCs) rather than bone marrow decreases the duration of neutropenia. Beyer et al. reported a randomized clinical trial that indicated that PBSCs mobilized with chemotherapy and G-CSF shortened the recovery time of engraftment to 10 days. Likewise, the use of PBSCs also has been evaluated in allogeneic transplant. Champlin et al. (2000) reported that the median time to engraftment was shortened to 14 days, versus 19 days with traditional bone marrow. Pavletic et al. also reported a significantly shorter time to neutrophil engraftment using PBSCs compared to bone marrow (10 versus 14 days, respectively). PBSCs have been shown to shorten the interval between transplant and neutrophil engraftment.

In recent years, nonmyeloablative preparative regimens have been used for allogeneic stem cell transplant. With a shorter neutropenic phase and less mucosal tissue damage, incidence of bacterial infections may be decreased during the early phase of transplant (Junghanss & Marr, 2002). Patients undergoing nonmyeloablative transplant regimens have not had fewer infections in later phases of the transplant process.

The dose of cells given also has attributed to the duration of neutropenia. Cell dose is commonly calculated based on the number of CD34+ cells. CD34+ is a molecule on the surface of primitive progenitor cells. These earliest cells are most valuable in reestablishing hematopoiesis post-transplant. Therefore, the number of CD34+ cells to be transplanted has become a marker for engraftment potential. Kiss et al. (1997) and Shulman, Birch, Zhen, Pania, and Weaver (1999) both reported research indicating that faster neutrophil engraftment time was associated with CD34+ cell infusions $> 5.0 \times 10^6$ cells per kilogram in autologous transplant. Kiss et al. and Shulman et al. also reported the decrease of one day ($p = 0.004$, $p = 0.0001$, respectively) in the median days to neutrophil engraftment. Shulman et al. equated a CD34+ cell dose of $> 5.0 \times 10^6$ cells per kilogram with a reduction in patient resource utilization, including fewer platelet and red blood cell (RBC) infusions, decreased length of stay in the hospital, decreased use of intravenous antibiotics and antifungal agents, and decreased days of G-CSF administration.

CD34+ cell doses also have been shown to affect the duration of neutropenia. Bittencourt et al. (2002) reported that a CD34+ cell dose of at least 3×10^6 cells per kilogram significantly decreased the neutropenic duration ($p = 0.04$). In this study, neutrophil engraftment occurred prior to day +60 in 97.1% of patients, with a dose of at least 3×10^6 CD34+ cells per kilogram. Neutrophil engraftment occurred prior to day +60 in only 93.1% of patients when the cell dose was less than

3×10^6 cells per kilogram. Umbilical cord blood (UCB) has been used as a source of stem cells for allogeneic transplant. Although UCB has been noted as a rich source of stem cells, the quantity of cells available for transplant from a single umbilical cord is small, making the use of UCB limited for adults.

The use of colony-stimulating factors, such as G-CSF and granulocyte macrophage–colony-stimulating factor (GM-CSF), has decreased the duration of neutropenia following HSCT, both autologous and allogeneic. In autologous transplant, the use of growth factors may decrease the time from transplant to neutrophil engraftment by as much as 5.5 days (Klumpp, Goldberg, & Mangan, 1995). In allogeneic HSCT, neutrophil recovery may be decreased by an average of four days with the use of G-CSF post-transplant (Bishop et al., 2000). Decreasing the period of neutropenia may lead to decreased incidence and/or severity of infectious complications.

In a study reported by Bishop et al. (2000), the time to neutrophil engraftment was shortened from 15 to 11 days ($p = 0.0082$) for a sample of patients receiving allogeneic transplant followed by the administration of filgrastim starting on the day of transplantation. Currently, optimal timing for growth factor administration post-transplant remains controversial. Researchers have reported starting G-CSF on days 1, 3, 5, 6, and 7 post-autologous transplant (de Azevedo et al., 2002). In studies, the significant differences of neutrophil recovery were associated with patients who were given G-CSF versus those that were not, rather than the day on which G-CSF was started. Although specific groups may benefit from beginning the G-CSF nearer to the transplant, other patient groups may tolerate the delayed start of growth factors without clinical compromise. In a study reported by Ener et al. (2001), there was no statistically significant difference in autologous transplant recipients' days to neutrophil engraftment or days spent in the hospital for the transplant. It is known that the administration of growth factors following autologous and allogeneic transplant significantly lessens the duration of neutropenia. The American Society of Clinical Oncology (1996) guidelines for using colony-stimulating factors recognize that growth factors improve hematopoietic recovery, although a specific schedule for administration is not recommended. Doses of G-CSF and GM-CSF following HSCT range from 5–10 mg/kg/day and typically are given subcutaneously, although the doses may be administered intravenously when necessary.

Prolonged neutrophil recovery or delayed engraftment may occur following HSCT. Anderson et al. (2003) reported that patients receiving allogeneic PBSCs had neutrophil recovery by 17 days post-HSCT, and those receiving marrow had neutrophil recovery at an average of 24 days post-HSCT. In this same

study, the incidence of bacteremia was higher in the marrow group (43%) versus the PBSC group (35%) at 100 days post-transplant.

The time from transplant to neutrophil engraftment is influenced by many factors. Studies have shown that the use of PBSCs versus bone marrow cells hastens the neutrophil recovery post-transplant. The use of colony-stimulating factors as well as non-myeloablative preparative regimens has shortened this interval as well. Because prolonged neutropenia increases the potential for infection, decreasing the interval between transplant and neutrophil engraftment directly impacts the patient's outcome.

Infections During the Transplantation Process

The duration of neutropenia is directly related to the risk of infection in transplant recipients. Infection is the most common cause of morbidity and mortality in the transplant population. Infections typically are discussed in the context of the period of time post-transplant that they occur. Different risk factors and organisms are associated with different phases of the transplant process. For patients undergoing allogeneic transplant, infection is the primary cause (15%) or a contributory (35%) cause of death (Passweg et al., 1998). The most common infections, their prevention, and treatment throughout the transplant process will be discussed.

The transplant process may be defined in phases beginning with pretransplant, followed by the immediate post-transplant or pre-engraftment phase (0–30 days), the intermediate post-transplant or post-engraftment phase (30–100 days), and the late post-transplant phase (after day 100) (CDC et al., 2000; Phillips, 1999; van Burik & Weisdorf, 1999). Infectious complications common during each phase of the transplant process are described in Table 7-2.

Pre-Engraftment

During the pre-engraftment phase, transplant recipients are at risk for infection because of severe myelosuppression-causing neutropenia and gastrointestinal mucosal toxicity, which occur as expected side effects of the preparative regimen. An additional risk is the interruption of skin integrity due to central venous catheters. Previous exposure to infections such as herpes simplex virus and cytomegalovirus (CMV) poses an additional risk, as reactivation is possible during the neutropenic phase.

All of these factors contribute to the development of infectious complications. Bacteria are the most common cause of infection during this period. The incidence of bacterial infections in this population may be as high as 100% (Buchsel, 1997). Common bacterial infection-causing pathogens include gram-negative *(Escherichia coli, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa)* and gram-positive *(Staphylococcus epidermitis, Staphylococcus aureus,* and *Streptococci)* species (Phillips, 1999; Walker & Burcat, 1997). The most common sites for infection include the oral mucosa and central venous catheters. Although prophylactic coverage is not recommended for the afebrile transplant patient (CDC et al., 2000), prophylaxis must be based on institutional-specific data. Common prophylactic interventions for the afebrile patient may include Pen-Vee K® (Wyeth Ayerst, Madison, NJ), Norfloxacin® (Merck, Whitehouse Station, NJ), and Bactrim® (Roche Pharmaceuticals, Nutley, NJ).

With the first febrile episode, these medications should be discontinued, and coverage for gram-positive and gram-negative organisms should be instituted. Common antibiotic therapies include third and fourth generation cephalosporins (nafcillin, Primaxin® [Merck], Merrem® [AstraZeneca, Wilmington, DE]) quinolones (Levaquin® [Ortho-McNeil Pharmaceutical, Raritan, NJ]), aminoglycosides (tobramycin, gentamycin, amikacin), and vancomycin. Because of the emergence of vancomycin-resistant enterococcus, vancomycin should not be used as prophylaxis (CDC et al.) and should be discontinued if culture sensitivity is not documented. In conjunction with the change or implementation of antibiotic therapy, the nurse should expect other diagnostic tests, including blood cultures, chest x-ray, stool, and urine cultures.

Yeast and fungal infections also may be problematic during this pre-engraftment phase. The two species commonly identified are *Candida albicans,* primarily as stomatitis, and *Aspergillus.* More recently, infections caused by less common amphotericin-resistant molds have been described, including non-fumigatus *Aspergillus* species, *Fusarium* species, and *Scedosporium* species (Marr, 2001; Marr, Carter, Crippa, Wald, & Corey, 2002). Prophylaxis for fungal infection may include medications such as fluconazole, itraconazole, or voriconazole. Common treatment of invasive fungal infections, such as *Aspergillus,* includes amphotericin B, liposomal amphotericin preparations, or voriconazole. Oral treatments such as nystatin and clotrimazole troches may be used to treat mucosal candidiasis. Patients should be instructed to prevent exposure to yeasts and molds by avoiding construction sites, building renovation areas, and gardening (CDC et al., 2000). In hospitals with transplant units, it is very important to minimize immunocompromised patient exposure to fungal risk factors. It is recommended that hospitals provide high-efficiency particulate air filtration (HEPA), positive air pressure between the patient rooms and hallways, appropriately sealed doors, windows, and outlets, more than 12 air exchanges per hour in the patient room, and barriers that prevent dust from crossing into patient areas during periods of construction or renovation (CDC et al.).

Reactivation of viral infections, such as herpes simplex virus (HSV) I and II, HHV-6, and CMV, also may occur during the immediate post-transplant phase. Patients and donors should be evaluated for latent viral infections prior to beginning a transplant procedure. Herpes simplex most often manifests as stomatitis. Prophylaxis with acyclovir or famciclovir is common in the pre-engraftment phase. Allogeneic HSCT recipients have a much higher incidence of CMV antigenemia than autologous HSCT recipients. Of the allogeneic patients, those with acute GVHD beyond grade I have a higher incidence of CMV (Osaro-giagbon, Defor, Weisdorf, Erice, & Weisdorf, 2000). The risk of CMV infection has been decreased to less than 3% in seronegative patients with the use of leukocyte filters for platelet and RBC transfusions. For seropositve patients, prophylaxis with ganciclovir, foscarnet, valacyclovir, or acyclovir is used in many HSCT centers (van Burik & Weisdorf, 1999). Ganciclovir is the standard treatment and prophylaxis for CMV; however, it may cause a decrease in WBC counts. Therefore, it is stopped just before transplant and restarted after engraftment. Screening for CMV should be performed for high-risk allogeneic patients at least one time per week from day 10 until day 100 post-transplant

Table 7-2. Infectious Complications and Occurrence in Hematopoietic Stem Cell Transplantation Recipients

ORGANISM	COMMON SITES	TREATMENT
FIRST MONTH POST-TRANSPLANT		
Viral		
Herpes simplex virus (HSV)	Oral, esophageal, skin, gastrointestinal (GI) tract, genital	Acyclovir, famciclovir
Respiratory syncytial virus (RSV)	Sinopulmonary	Aerosolized ribavirin
Epstein-Barr virus (EBV)	Oral, esophageal, skin, GI tract	Treatment usually is not indicated.
Bacterial		
Gram + *(S. epidermidis, S. aureus, Streptococci)*	Skin, blood, sinopulmonary	Third and fourth generation cephalosporins, quinolones, aminoglycosides, vancomycin
Gram – *(E. coli, P. aeruginosa, Klebsiella)*	GI, blood, oral, perirectal	
Fungal		
Candida species *(C. albicans,* glabrata krusei)	Oral, esophageal, skin	Fluconazole, voriconazole, itraconazole, amphotericin B, liposomal amphotericin
Aspergillus (fumagata, flavum)	Sinopulmonary	
ONE TO FOUR MONTHS POST-TRANSPLANT		
Viral		
Cytomegalovirus (CMV)	Pulmonary, hepatic, GI	Ganciclovir, foscarnet, valacyclovir, acyclovir
Enteric viruses (rotavirus, Coxsackie, adenovirus)	Pulmonary, urinary, GI, hepatic	No specific treatment
RSV	Sinopulmonary	Aerosolized ribavirin
Parainfluenza	Pulmonary	Possibly ribavirin, but no standard treatment
Bacterial		
Gram +	Sinopulmonary	Third and fourth generation cephalosporins, quinolones, aminoglycosides, vancomycin
Fungal		
Candida species	Oral, hepatosplenic, integument	Fluconazole, voriconazole, itraconazole, amphotericin B, liposomal amphotericin
Aspergillus species	Sinopulmonary, central nervous system (CNS)	
Mucormycosis	Sinopulmonary	
Coccidioides	Sinopulmonary	
Cryptococcus neoformans	Pulmonary, CNS	
Protozoan		
Pneumocystis carinii	Pulmonary	Standard is trimethoprim-sulfamethoxazole (TMP-SMZ). Pentamidine, atovaquone may be used if allergic to sulfa.
Toxoplasma gondii	Pulmonary, CNS	Pyrimethamine and sulfonamides may be combined with clindamycin and spiramycin, especially if sulfa allergy.
4–12 MONTHS POST-TRANSPLANT		
Viral		
CMV, echoviruses, RSV, Varicella zoster (VCV)	Integument, pulmonary, hepatic	CMV—ganciclovir, foscarnet, valacyclovir, acyclovir RSV—aerosolized ribavirin VCV—acyclovir, valacyclovir, famciclovir Echoviruses—no specific treatment, IVIG
Bacterial		
Gram + *(S. pneumoniae, H. influenza, Pneumococci)*	Sinopulmonary, blood	Third and fourth generation cephalosporins, quinolones, aminoglycosides, vancomycin
Fungal		
Aspergillus	Sinopulmonary	Fluconazole, voriconazole, itraconazole, amphotericin B, liposomal amphotericin
Coccidioides	Sinopulmonary	
Protozoan		
Pneumocystis carinii	Pulmonary	Standard is TMP-SMZ. Pentamidine, atovaquone may be used if allergic to sulfa.
Toxoplasma gondii	Pulmonary, CNS	Pyrimethamine and sulfonamides may be combined with clindamycin and spiramycin, especially if sulfa allergy.

(Continued on next page)

Table 7-2. Infectious Complications and Occurrence in Hematopoietic Stem Cell Transplantation Recipients (Continued)

ORGANISM	COMMON SITES	TREATMENT
GREATER THAN 12 MONTHS POST-TRANSPLANT		
Viral		
VZV	Integument	Acyclovir, valacyclovir, famciclovir
Bacterial		
Gram + (*Streptococci, H. Influenza,* encapsulated bacteria)	Sinopulmonary, blood	Third and fourth generation cephalosporins, quinolones, aminoglycosides, vancomycin

Note. Based on information from Barnes 1998a, 1998b; Prentice et al., 1998; Riley, 1998; Shapiro et al., 1997; Westmoreland, 1998.

(CDC et al., 2000). Seropositive autologous patients who are being treated for hematologic malignancies should be tested for CMV reactivation weekly until 60 days post-transplant. Only autologous patients with CMV antigenemia or those who received a CD34+ selected transplant product should be treated with ganciclovir or foscarnet. Varicella zoster virus (VZV) and HSV are treated with acyclovir, valacyclovir, or famciclovir. Evaluating patients and donors for the presence of viruses prior to transplant provides a baseline for prophylaxis and treatment of the patient post-transplant. Testing for CMV is primarily performed through antigen detection techniques (Boeckh & Boivin, 1998), with the most common being the hybrid capture technique. Antigen detection techniques are less expensive and more specific in detecting early CMV.

In the allogeneic patient population, prophylactic treatment for *Pneumocystis carinii* pneumonia (PCP) with trimethoprimsulfamethoxazole (TMP-SMZ) is recommended beginning pretransplant and continuing until the patient is no longer being treated for chronic GVHD (CDC et al., 2000). If the patient has an allergy to sulfa, pentamidine or atovaquone may be used. TMP-SMZ should be discontinued during the neutropenic period because a side effect of the medication is a decrease in WBC counts. During this time, pentamidine or atovaquone may be used as prophylaxis.

Other measures that are important to preventing early infections are the use of air filtration systems, such as HEPA or laminar airflow. Although these systems have been shown to be effective in significantly lowering the infection rates of allogeneic bone marrow transplant recipients (Passweg et al., 1998), this may not be necessary for all HSCT recipients. Russell et al. (2000) noted that strict isolation policies may not add significant protection against infection. As healthcare patterns have shifted and many patients are receiving treatment in the home or outpatient clinics, air filtration systems are not commonly used for autologous HSCT patients. Selected patients treated outside of filtered hospital rooms may not be at higher risk for infection during the pre-engraftment phase of transplant (Herrmann, Trent, Cooney, & Cannell, 1999). Likewise, carefully selected patients treated in the outpatient environment may use approximately the same amount of antibiotic treatment and develop fevers at approximately the same rate as those in inpatient settings (Meisenberg et al., 1998). Perhaps more important than air filtration systems is the patient's and family's understanding of appropriate hygiene, mouth care, care of indwelling central

venous catheters, appropriate low bacterial diets, and avoidance of crowds, fresh flowers or plants, and other sources of bacterial contamination. Although the literature does not support one anti-infection regimen at this time, it is vitally important that patients with neutropenia and fever be treated immediately and proactively to prevent life-threatening complications (Phillips, 1999). Allowing treatment in the outpatient setting or sending patients out of the hospital prior to engraftment may improve the patient's emotional and social outlook without compromising safety. It is important that patients be carefully selected for programs allowing for this flexibility.

Postengraftment

In the postengraftment phase, differences between allogeneic and autologous transplants become more evident. For autologous patients, the risk of developing infectious complications decreases during the intermediate post-transplant or postengraftment phase, but infection occurs. However, for the allogeneic patient, risk factors such as GVHD, graft rejection, prolonged neutropenia, and continued immunosuppressive therapy cause a continued threat of infection (Phillips, 1999; Walker & Burcat, 1997). During this time, patients are especially at risk for nonbacterial infections, such as viral and fungal infections, although the threat of bacterial infection continues. Interstitial pneumonia (IP) that is often caused by a virus (CMV, HSV, parainfluenza, or respiratory syncytial virus) is more common between days 30 and 100 post-transplant (see chapter on cardiopulmonary effects for more discussion of IP) (Shapiro, Davison, & Rust, 1997). Localized or disseminated VZV infections also are seen during this phase. Treatment for zoster infections because of reactivation or a primary infection includes use of high-dose acyclovir. Fortunately, an often fatal infectious complication, *Pneumocystis carinii* pneumonia, has been essentially eliminated from the repertoire of postengraftment complications by the prophylactic administration of TMP-SMZ or pentamidine postengraftment (Walker & Burcat).

Nursing care of the patient during the postengraftment phase of HSCT includes frequent and thorough assessment, including central venous catheter sites, respiratory status, vital signs, and administration of antibiotics, antifungals, and antiviral medications. Only a few years ago, HSCT patients with infections in the intermediate post-transplant phase would be hospitalized. Currently, it is common for both allogeneic and autologous patients

to be cared for in the home by homecare nurses and family members. Nursing care may revolve around education of the patient and caregivers. Teaching the patient and caregiver(s) the signs and symptoms of infection; accurate assessment of temperature, skin, and mucosal linings; and the use of interventions to minimize the risk of infection (e.g., hand washing, clean environment, medication administration) are often the most important nursing interventions during this phase of the HSCT process.

Late Post-Transplant

The final phase of the HSCT process is the late post-transplant phase. At this point, most patients will have engraftment of WBCs, healing of mucosal linings, and adequate skin integrity. Patients without ongoing complications of HSCT are not significantly at risk for major infectious complications. Patients with ongoing complications, such as GVHD, graft rejection or failure, or relapse or progression of disease, may continue to be more at risk for infectious complications. Common infections during this time are *Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitidis,* sinusitis, and VZV (Buchsel, 1997; Phillips, 1999; van Burik & Weisdorf, 1999).

During the final phase of transplant, ongoing patient and caregiver education is imperative. These patients may be seen only on rare occasions, if at all, by the transplant team because of financial constraints, distance from the transplant center, or transportation limitations. It is necessary for nurses to provide education to the patient and caregivers regarding assessment and appropriate interventions for infectious complications, and it is also imperative that HSCT nurses share details of the patient's transplant course and information concerning appropriate monitoring and referral with the nurses and physicians who will resume care of the patient away from the transplant center. For patients still being seen by the transplant team, nursing care continues to include education, assessment, and administration of appropriate medications and interventions.

Thrombocytopenia

Thrombocytopenia is defined as an abnormal decrease in the number of circulating platelets (Whedon & Wujcik, 1997). Platelets are small fragments derived from megakaryocytes in the bone marrow. Under normal, healthy conditions, approximately 30,000 platelets/mm³ are formed each day. The production of platelets is regulated by a hormone-like substance called thrombopoietin, which is produced by the kidneys. Platelets are removed by the spleen if not used after approximately 10 days. Platelets are crucial for hemostasis and preventing hemorrhage or bleeding and also for maintaining vascular integrity in the absence of injury (Rutherford & Frenkel, 1994).

Thrombocytopenia commonly occurs in the post-transplant patient because of severe myelosuppression resulting from the preparative regimen of chemotherapy, immunotherapy, and/or radiation therapy (Whedon & Wujcik, 1997). Megakaryocytes are typically the last cell line to engraft following both autologous and allogeneic stem cell transplantation (Shapiro et al., 1997), although the engraftment period is shorter following PBSC transplantation (Ezzone, 1997). Normal platelet counts are not achieved for approximately one to three months following

stem cell transplantation (Shapiro et al.). Persistent and chronic thrombocytopenia can indicate a poor prognosis for the patient (Dominietto et al., 2001). Thrombocytopenia may reoccur later in the post-transplant phase, after an initial recovery, because of viral infections, GVHD, delayed engraftment, and drug toxicity (Deeg, 1990; Shapiro et al.).

Although controversy exists about the platelet count threshold at which prophylactic transfusions are beneficial (Beutler, 1993; Labovich, 1997), most institutions use the criteria of petechiae, overt bleeding, increased bruising, and a platelet count less than 20,000 as a trigger for platelet transfusions. Severity of thrombocytopenia is graded using the National Cancer Institute Common Toxicity Criteria (see Table 7-3).

Thrombocytopenia can result from any mechanism that affects platelets: the use of prophylactic heparin for veno-occlusive disease (VOD), defective or suppressed production of platelets, abnormal distribution of platelets, or accelerated platelet destruction or consumption (Belcher, 1993). The suppressed production of platelets is a common sequela of direct exposure to preparative regimens utilizing toxic antineoplastic agents and/or radiation therapy. There is a reduction in platelet count following exposure to antineoplastic therapies, a period of nadir followed by recovery. As the existing circulating platelets age and die, they are removed from the circulation through natural processes. They are not replaced because of the destructive impact of the therapy on cycling, differentiating precursor cells (Belcher). There is a lag between generations of hematopoietic cells that correspond to the period of lowest counts (the nadir) (Groenwald, Frogge, Goodman, & Yarbro, 1997).

Antineoplastic agents used in the preparative regimens of both allogeneic and autologous stem cell transplantation commonly cause myelosuppressive effects, such as thrombocytopenia. These agents include busulfan, carmustine, melphalan, cyclophosphamide, etoposide, thiotepa, carboplatin, cisplatin, cytarabine, and total body irradiation (Ezzone, 1997). Atrophy and fibrosis of bone marrow are late effects of chemotherapy and radiation therapy and may predispose transplant recipients to delayed and chronic thrombocytopenia (Deeg, 1990). In a study by Dominietto et al. (2001), thrombocytopenia correlated with poor transplant outcomes at 30-day, 60-day, and 180-day intervals in the allogeneic transplant setting.

In healthy individuals, approximately one-third of the total platelet volume is sequestered within the spleen (George & Rizvi, 2001). Thrombocytopenia that results from abnormal distribution is related to splenomegaly. An abnormally large number of platelets are sequestered in the spleen with this disorder. This disorder also may be seen in patients with vari-

Table 7-3. Grading of Thrombocytopenia Using the National Cancer Institute Common Toxicity Criteria

GRADE	0	1	2	3	4
Platelets (X 10⁹)	–	50–75	20–50	10–20	< 10

Note. Based on information from the National Cancer Institute, 1999.

ous types of lymphomas and those with portal hypertension (Belcher, 1993).

Fever and systemic infection are processes that may cause thrombocytopenia through accelerated destruction and/or consumptive processes. Viral infections, including CMV, Epstein-Barr virus, HHV-6, Hantavirus, and HIV, commonly cause thrombocytopenia. Other infectious diseases that cause thrombocytopenia via these processes include mycoplasma and mycobacteria (George, Vesely, & Rizvi, 2001).

Drugs such as NSAIDs, aspirin, and aspirin-containing products cause disorders of platelet function. Other drugs such as Bactrim, heparin, quinine, and quinidine are thought to cause thrombocytopenia through an immune-mediated complex (George et al., 2001). Other drugs that may be implicated in thrombocytopenia in the transplant recipient include cyclosporine A, ganciclovir (Shapiro et al., 1997), digoxin, furosemide, penicillin, vancomycin, and phenytoin (Shuey, 1996). These agents are commonly used in the allogeneic transplant setting (Shapiro et al.).

A complication of severe thrombocytopenia in the transplant recipient may be diffuse alveolar hemorrhage (DAH) (Armitage & Antman, 1992). *Aspergillus* pneumonia also may be a contributing factor resulting in alveolar hemorrhage. The onset of DAH correlates with the onset of WBC recovery. DAH is recognized on bronchoalveolar lavage when sequential instillation and aspiration of normal saline results in recovered fluid that becomes progressively bloodier with each recovered aliquot. Symptoms include dyspnea, diffuse consolidation on chest x-ray, high fevers, severe mucositis, and renal insufficiency. The majority of patients eventually require mechanical ventilation. DAH can proceed to death in more than 75% of patients. High-dose corticosteroids are commonly used for treatment (Armitage & Antman).

Another complication of thrombocytopenia is thrombotic thrombocytopenia purpura/hemolytic uremic syndrome (TTP/HUS). Initially described as a distinct disorder, TTP/HUS is more recently being recognized as a single clinical syndrome that can best be characterized as a spectrum of disorders (George et al., 2001). This syndrome has become more widely recognized in the post-transplant population during the last 15 years (Uderzo et al., 2000). Earlier descriptions of this syndrome included microangiopathic hemolytic anemia, thrombocytopenia, neurologic symptoms, renal function abnormalities, and fever. Currently, only the criteria of thrombocytopenia and microangiopathic hemolytic anemia, without other clinically apparent cause, are sufficient to establish this diagnosis (George et al.).

The pathophysiology of TTP/HUS is a vascular endothelial injury resulting in the release of von Willebrand factors and vascular micro-thrombi. Symptoms result from reversible platelet thrombus formation within the microvasculature, leading to transient ischemia of the brain, kidneys, and other organs (Moake & Byrnes, 1996). This disorder has been described as early as 2–3 months post-transplant and as late as 11 months post-HSCT. TTP/HUS may have multiple etiologies, including drug toxicity, infection, autoimmune processes, and bone marrow transplantation (George et al., 2001).

TTP/HUS has been problematic to recognize because the complications in the critically ill post-HSCT recipient can be similar (George et al., 2001). The factors that positively correlate with TTP/HUS include recipients of transplants from matched, unrelated donors and HLA-antigen mismatched donors, GVHD, total body irradiation as part of the preparative regimen, and infections. Nephrotoxicity and neurotoxicity associated with cyclosporine use also may be a complicated finding (George et al.).

Although the diagnosis of TTP/HUS should be suspected in the presence of microangiopathic hemolytic anemia and thrombocytopenia, most patients also present with renal and neurologic abnormalities. Symptoms may include aphasia, confusion, memory loss, paresis, and behavioral changes. Patients also may complain of abdominal symptoms: pain, nausea, vomiting, and diarrhea. The laboratory findings include thrombocytopenia, the appearance of shistocytes on peripheral blood smear, high serum LDH levels with isoenzymes reflecting hemolysis, and ischemic injury to multiple organs (George et al., 2001).

If not recognized and treated promptly, this syndrome can be fatal. The treatment for this disorder is plasma volume exchange and treating the underlying cause. Once the diagnosis is made, emergency plasma volume exchange is performed daily until the platelet count and LDH levels normalize and are stable for three days (BRT Laboratories, 2000). Unless there is severe, life-threatening bleeding, platelet transfusions are contraindicated, as they may contribute to the formation of microthrombi (Moake & Byrnes, 1996).

The apheresis process that healthy stem cell donors and autologous transplant recipients undergo may cause some transient thrombocytopenia. Studies have demonstrated a significant reduction in platelet counts during mobilization and collection of stem cells. These effects are transient, and donors' platelet counts returned to normal within a few days without transfusions. The mechanism for this phenomenon is not known (Wagner & Quinones, 1999; Walker, Roethke, & Martin, 1994).

Management of thrombocytopenia in the stem cell transplant recipient includes preventive measures, supportive care, and platelet transfusions. Prevention of bleeding is crucial. In the setting of thrombocytopenia, the most common sites of bleeding may be the mucous membranes, skin, gastrointestinal system, genitourinary system, respiratory tract, and intracranial compartment.

Preventive nursing management for transplant recipients during this time includes teaching patients to use very soft bristle toothbrushes or sponges when performing mouth care to prevent trauma and bleeding at the mucous membranes. Other measures to prevent trauma to mucous membranes include avoiding the use of rectal thermometers and rectal suppositories. Stool softeners may be used, and patients are encouraged to liberalize fluid intake to prevent constipation. Patients should be routinely monitored for nosebleeds, melanotic stools, and hematuria, as well as for occult bleeding in emesis, urine, and stool. Menstruating females are typically begun on hormone therapy to prevent vaginal bleeding of menstruation.

The U.S. Food and Drug Administration recently approved Neumega® (Wyeth), a thrombopoietic growth factor, for the prevention of severe thrombocytopenia following myelosuppressive chemotherapy in patients with nonmyeloid malignancies (Rust, Wood, & Battiato, 1999). This agent may have limited use in the transplant population because of the exclusion of its use in nonmyeloid malignancies. The side effects of this agent, including

edema, dyspnea, and tachycardia, also may limit its usefulness. Although prophylactic platelet transfusions are controversial (Beutler, 1993), most transplant programs designate a minimum threshold as a trigger for platelet transfusion. Earlier studies indicated that hemorrhage was seen more frequently and with greater severity when the platelet counts were less than 10,000/mm³. The same studies also indicated that gross visible hemorrhage rarely occurred with platelet counts greater than 20,000/mm³ (Fuller, 1990). Thus, the 20,000/mm³ threshold served as a trigger for initiating prophylactic platelet transfusion to prevent hemorrhage (Groenwald et al., 1997). Others suggested that prophylactic transfusions lead to sensitizing the patient to antigens found on platelets (alloimmunization), with subsequent inability to control hemorrhage when it occurred (Beutler; Fuller). Patients with thrombocytopenia who are actively bleeding require an aggressive approach to platelet transfusions and may be transfused for platelet counts less than 50,000/mm³ (Fuller). Patients on heparin for VOD prophylaxis may be kept at a higher threshold, 30,000/mm³, because of an increased incidence of bleeding.

Platelets for transfusion are obtained from one of two sources (Fuller, 1990; Triulzi, 2000): multiple, random donors or an HLA-matched single donor. Random donor platelets are pooled from the blood of several different donors. One unit of blood typically yields one unit of platelets. These are more readily available and less expensive. However, this source of platelets exposes the patient to several different donors, increasing the risk of developing transfusion transmitted disease and alloimmunization (Beutler, 1993; Fuller). Single-donor platelets are derived from an individual through apheresis. The donor platelets are harvested while the RBCs are returned during the apheresis procedure. This process yields 6–10 units of transfusable platelets (Fuller).

Alloimmunization is associated with multiple transfusions for which transplant recipients are at risk. When alloimmunization occurs, platelet antibodies attack transfused platelets and may cause platelet levels to decrease after transfusions. There appears to be a dose response pattern for the development of alloimmunization. The more antigens the recipient is exposed to through multiple units of donor-derived blood and platelets, the more at risk the recipient is to develop alloimmunization (Labovich, 1997). For this reason, some would recommend that transplant recipients should only receive single-donor and/or HLA-matched platelets. Further, the discussion is raised that patients who are potential transplant candidates should *only* receive single-donor or HLA-matched platelet transfusions (Armitage & Antman, 1992; Fuller, 1990). Patients in whom alloimmunization is suspected should be tested by determining platelet count levels with serial blood draws after platelet transfusions. Blood tests are available to detect platelet refractory antiplatelet antibodies—cytotoxic anti-HLA antibodies. Alloimmunization risk can be minimized or delayed by the use of special filters that remove leukocytes from blood products before transfusion (Triulzi, 2000).

Anemia

Anemia is defined as a decrease in RBCs or the hemoglobin level that results in the reduction of oxygen-carrying capacity of blood (Erickson, 1996; Loney & Chernecky, 2000). Erythropoietin, an erythrocyte growth factor, is produced or suppressed based on a feedback mechanism involving oxygen tension. The kidneys produce more than 90% of the body's erythropoietin. When oxygen tension drops, interstitial renal cell and central vein hepatocyte receptors signal expression of an erythropoietin gene, resulting in erythropoietin production. As erythropoietin enters the systemic circulation, it quickly stimulates erythrocyte precursor cells in the bone marrow to accelerate RBC production and maturation (Loney & Chernecky). To keep the RBC mass stable, the bone marrow must produce and release approximately 2.5 billion RBCs per kg of body weight each day. The life span of the RBC is approximately 120 days.

Anemia may result from a decrease in RBC production, an increase in RBC destruction, or loss of RBCs through hemorrhage (see Table 7-4). Anemia also may be caused by the direct toxic effect of chemotherapy on the kidney resulting in an inability to respond to the stimulation of erythropoietin (Gillespie, 2002; Groopman & Itri, 1999; Rogers, 2002). Grading the severity of anemia may be described utilizing the National Cancer Institute and World Health Organization toxicity scales (see Table 7-5).

Anemia in the transplant recipient has several causative factors. These include hemolysis, malignancy type, blood loss

Table 7-4. Bleeding Complications and Etiologies That May Contribute to Anemia in the Transplant Recipient

PATHOPHYSIOLOGY	ETIOLOGY	SIGNS/SYMPTOMS	MANAGEMENT
• Myelosuppression induced by preparative regimen • Delayed platelet engraftment • Marrow suppressive medications • Coagulation abnormalities • Platelet autoantibodies • Graft rejection	• Graft versus host disease • Cyclosporine • Veno-occlusive disease • Altered mucosal barriers • Delayed/failed engraftment • Viral infection • ABO-incompatible bone marrow transplantation	Skin/mucosa: petechiae, ecchymoses, bruising, scleral hemorrhage Genitourinary: hematuria, menorrhagia Gastrointestinal: guaiac-positive stool/emesis, abdominal distension or discomfort Pulmonary: epistaxis, hemoptysis, change in breathing pattern Intracranial: headache, restlessness, change in pupil response, seizure, change in mental status/level of consciousness	Perform frequent assessment. Monitor hemoglobin/hematocrit, platelets, and coagulation studies. Minimize blood loss. Administer blood products. Avoid medications that inhibit platelet production and/or function. Avoid invasive procedures. Follow bleeding precautions.

Note. Based on information from Ezzone, 1997.

Table 7-5. Anemia Toxicity Scales

GRADE	SEVERITY	NATIONAL CANCER INSTITUTE SCALE	WORLD HEALTH ORGANIZATION SCALE
0	None	Normal limits*	> 11
1	Mild	10–normal	9.5–10
2	Moderate	8–10	8–9.4
3	Severe	6.5–7.9	6.5–7.9
4	Life threatening	< 6.5	< 6.5

*14–18 g/dl for men; 12–16 g/dl for women
Note. Based on information from Groopman & Itri, 1999.

due to bleeding, suppression of bone marrow function caused by antineoplastic agents and radiation therapy, nutritional deficiency, and kidney failure caused by antineoplastic agents as well as other drugs. For the transplant recipient, these factors may be complex and overlapping.

Chemotherapy agents used in the preparative regimens of transplant recipients suppress bone marrow function, including erythropoiesis, and can lead to poor dietary intake of iron and vitamins and cause RBC lysis and microangiopathic bleeding. All these mechanisms overlap to produce anemia in the transplant recipient.

The suppressive effects of intensive chemotherapy and radiation on the hematopoietic function of bone marrow are well documented. Radiation exposure results in a decrease in the production of RBCs when bone marrow–producing areas, such as the pelvis, sternum, and proximal ends of long bones, are included in the radiation field. Many of the drugs used in the transplant setting in addition to chemotherapeutic agents may be toxic to the kidneys, further compromising erythropoiesis (Franco & Gould, 1994; Groenwald et al., 1997; Whedon & Wujcik, 1997).

Immune hemolytic anemia is a complication of hematopoietic cell transplantation (Sniecinski & O'Donnell, 1999). The majority of these cases are due to ABO-RBC antigen incompatibilities between donor and recipient. The incidence may be as high as one-third of all allogeneic cell transplants. The incompatibilities can be minor or major. Donor-recipient ABO incompatibility is not a contraindication to successful transplantation, and there is no significant adverse impact on the incidence of graft rejection, GVHD, or survival. However, patients undergoing ABO-incompatible transplant are at risk for development of several complications (see Figure 7-1). Major ABO incompatibilities between donor and recipient have the potential for severe hemolytic reaction during marrow or peripheral blood infusion. At the least, incompatibilities could lead to delayed erythropoiesis and/or persistent hemolysis post-transplant (Sniecinski & O'Donnell).

Prevention strategies include removal of the incompatible RBCs from marrow aspirate before infusion. The RBC content in PBSC concentrate is less than in the marrow aspirate but may be sufficient to cause hemolysis at the time of the infusion (Sniecinski & O'Donnell, 1999).

Leukemias, lymphomas, multiple myelomas, and myelodysplastic syndromes are the cancers associated most frequently with anemia (Rogers, 2002). These also are among the most frequently transplanted malignant diseases (International Bone Marrow

Transplant Registry/Autologous Blood and Marrow Transplant Registry, 2003). Some tumors possess factors that cause myelosuppression directly, which causes anemia (Rogers).

Prior myelosuppressive drug therapy, particularly platinum-derived agents, may have a cumulative impairment on erythropoiesis (Groopman & Itri, 1999). The intensive preparative conditioning regimens in the transplant setting create a hypoproliferative anemia because of the myelosuppressive effects on the bone marrow (Gillespie, 2002).

Transplant recipients commonly experience nausea and/or vomiting and mucositis as side effects of the preparative conditioning regimens. The intake of essential nutrients, including iron, folate, and vitamin B_{12}, for the normal differentiation and proliferation of erythroid progenitor cells is thus insufficient. The inability to take in adequate nutrients is compromised, adding another complicating factor for the development of anemia (Rogers, 2002).

Finally, acute hemolysis caused by cyclosporine A, Prograf® (Fujisawa, Chantilly, VA), ABO-incompatible graft, infection, or hemolytic uremic syndrome may cause bleeding, leading to anemia in the post-transplant recipient (Shapiro et. al., 1997).

The clinical features of anemia include fatigue, pallor and shortness of breath, headaches, dizziness and decreased cognition, sleep disorders, and sexual dysfunction (Gillespie, 2002). Hypotension and orthostasis may be present in the setting of an acute drop in hematocrit (Shapiro et. al., 1997).

The management of anemia in the transplant recipient includes anticipation of risk factors and initiating strategies to minimize risk to the patient. RBC transfusions should be anticipated to correct hemoglobin during the acute phases of transplant. Diagnostic studies include daily hemoglobin and hematocrit counts throughout the period of aplasia. These determinations are obtained more frequently if the patient is actively bleeding. Guaiac of emesis and stool and dipstick of urine for heme are important and appropriate nursing measures. The hemolysis workup includes urinalysis, complete blood count (CBC), haptoglobin, lactate dehydrogenase, direct and indirect Coombs' test, and fractionated bilirubin (Shapiro et al., 1997).

Major ABO incompatibility
- Immediate hemolysis of the red blood cells (RBCs) infused with donor marrow
- Delayed hemolysis of RBCs produced by engrafted marrow
- Delayed onset of erythropoiesis
- Pure red cell aplasia

Minor ABO incompatibility
- Immediate hemolysis of recipient RBCs by infused marrow
- Delayed hemolysis of recipient RBCs due to persistent production of marrow lymphocytes

Major and minor ABO incompatibility
- Immediate hemolysis caused by recipient and/or donor
- Delayed hemolysis caused by recipient and/or donor

Figure 7-1. Complications of ABO-Incompatible Bone Marrow Transplantation

Note. Based on information from Sniecinski & O'Donnell, 1999.

Tachycardia, tachypnea, hypotension, dyspnea at rest, and other symptoms of tissue hypoxia may occur as anemia becomes more severe (Erickson, 1996). The decision to transfuse RBCs is based upon hemoglobin concentration and the presence of signs or symptoms of anemia. Generally, when the hemoglobin is less than 8 g/dl and signs or symptoms of anemia may be present, transfusion is required. However, patients with underlying cardiopulmonary compromise and older adults (Rogers, 2002) may require transfusions at higher hemoglobin thresholds (Rieger & Haeuber, 1995). One unit of packed RBCs (10–15 ml/kg in pediatric patients) can raise the hemoglobin increment by 1 g/dl (Shapiro et al., 1997).

An alternative or possible additive therapy made available in recent years has been recombinant erythropoietin alfa. Over a 12-week study, this agent was shown to increase hematocrit and decrease transfusion requirements and lead to the indication for its use in chemotherapy-induced anemia (Rieger & Haeuber, 1995). This agent may be given as a subcutaneous injection or intravenously weekly in the ambulatory treatment setting. Some side effects include hypertension and flu-like symptoms (Rieger & Haeuber).

Management Strategies for Anemia and Thrombocytopenia

Patients undergoing autologous or allogeneic stem cell transplantation will require multiple transfusions of platelets and packed RBCs during the period of aplasia following transplant, until stable recovery of hematopoiesis. Although component therapy is significantly safer now than in the past, there are still notable risks associated with transfusion therapy (Labovich, 1997). Three of those transfusion-related risks that will be discussed include infectious disease transmission, alloimmunization, and febrile nonhemolytic transfusion reactions.

The most notable transfusion-related risk is that of infectious disease transmission. Viruses with the potential for transmission include hepatitis A, B, and C, HIV, human T cell leukemia virus-1, parvovirus B19, Epstein-Barr virus, and CMV (Guertler, 2002). Bacterial and protozoal agents also have transmissible potential through the blood supply (Chamberland, 2002). However, leukofiltration and other measures have reduced the risk of disease transmission in recent years. With the current methods now employed, the estimated risk for infection by screened blood components in Europe and the United States is 1 in 50,000–1.6 million transfused components (Vreilink & Reesink, 1998).

Another transfusion-related complication in the transplant recipient includes the risk of alloimmunization. Alloimmunization occurs when patients develop antibodies that destroy transfused blood components, most commonly platelets. This occurs as a consequence of being exposed to multiple transfusions over time (Labovich, 1997). The significant risk of alloimmunization is that it may lead to refractory thrombocytopenia, which is difficult to treat (Rowe et al., 1994). The use of leukofiltered platelets, single-donor platelets, and irradiated platelets minimizes this risk to the patient (Rowe et al.).

Febrile, nonhemolytic reactions are unexplained temperature increases of > 1°C or 2°F from baseline or the onset of chills or rigors in the patient who is receiving a transfusion. This may develop in patients within four to six hours of completing the transfusion. These reactions are the most common complication of platelet transfusions (Baldwin, 2002). Risk factors include previous transfusions, previous febrile reactions, and hematologic malignancy. Leukocyte reduction of all transfused blood products reduces the incidence of febrile nonhemolytic transfusions.

Commonly in the acute phases of transplantation, patients receive a transfusion of packed RBCs to correct hemoglobin deficits. A commonly used threshold for prophylactic transfusion of RBCs is ≤ 8 g/dl (Plaza, 2000). Pharmaceutical agents that may be useful for the management of chronic anemia include erythropoietin alfa and darbepoetin alfa. These agents are effective in increasing hemoglobin levels and decreasing the number of transfusions required. Erythropoietin alfa is dosed subcutaneously but can be administered intravenously. It is customarily dosed at 40,000 units as a weekly subcutaneous injection. The median time to response is 4 weeks, but 12 weeks may be needed to determine if the patient is responsive to therapy.

Darbepoetin alfa is a long-acting agent that stimulates erythropoiesis. The mean half-life is three times longer than epoetin alfa. This allows for less frequent dosing. A darbepoetin alfa dose of 3 mcg/kg given every two weeks produced similar hematopoietic responses to epoetin alfa dosed at 40,000–60,000 units weekly (Glaspy et al., 2002; Pirker & Smith, 2002).

Some transplant patients may need a higher threshold trigger for prophylactic platelet transfusion. This would include patients who are on chronic anticoagulation therapy and patients who are on mechanical ventilation and are frequently being suctioned.

Delayed Engraftment

Delayed engraftment and graft failure refer to the lack of functional hematopoiesis after marrow transplantation. Primary graft failure is the failure to establish hematopoiesis (Whedon & Wujcik, 1997). In autologous transplants, this may be because of inadequate volume, a defect in the quality of stem cells, cryopreservation, or damage during collection of cells (Shapiro et al., 1997; Whedon & Wujcik). In allogeneic transplants, graft failure is more commonly seen with HLA-mismatched donor marrow, cord blood transplant, or transplantation with T cell–depleted bone marrow (Lum, 1990).

Diagnostic studies include at least daily CBC with differential and platelets to follow engraftment trends and to evaluate transfusion needs. Bone marrow aspirate and biopsy and cytogenetics studies often are used to evaluate chimerism (Shapiro et al., 1997). Management of graft failure may include discontinuation of drugs known to be myelosuppressive (e.g., ganciclovir, Bactrim). Reinfusion of allogeneic marrow, back-up marrow with or without further conditioning, or attempted stimulation with colony-stimulating factors are all possible strategies (Shapiro et al.).

Conclusion

Hematologic and infectious complications are complex and all too common occurrences in the patient undergoing HSCT. Nurses traditionally have held key responsibility for symptom identification and management (Gillespie, 2002). Aggressive, proactive nursing care is critical in helping patients through

these dangerous phases of the post-transplant period. A well-rounded grasp of current knowledge is essential to maintaining skills required to anticipate these complications and intervene early and effectively.

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