Transfusion support for patients with cancer is a complex, multifaceted medical therapy meant to assist in the management of complications related to chemotherapy, radiation, transplantation, or widespread metastatic disease. Oncology patients often require chronic transfusion support and present several unique challenges to the provider. For these patients, greater attention must be paid to the selection, preparation, modification, and response to blood components to help ensure better outcomes. This chapter highlights the most challenging aspects of transfusion therapy for oncology patients encountered by clinicians and transfusion services on a routine basis.

**Red cell transfusion**

**Indications**

The goal of red blood cell (RBC) transfusion in oncology patients is the same as in other populations—to increase the oxygen carrying capacity of whole blood for patients with anemia. Unfortunately, there are no evidence-based laboratory criteria upon which to determine when transfusion is appropriate for oncology patients. Studies in other critically ill patient populations have shown that hemoglobin levels of 7 to 10 g/dL can be tolerated without the need for allogeneic transfusion. There is no evidence to suggest that higher hemoglobin levels provide any therapeutic benefit. Indeed, there is evidence to suggest that “hypertransfusion” may actually be detrimental to patient outcomes. Therefore, oncology patients should be transfused for symptomatic anemia or at predetermined hemoglobin or hematocrit levels defined by a hospital’s oncology service.

**Selection of ABO group for RBC transfusion**

For most oncology patients, no special consideration is needed for the appropriate selection of ABO group for RBC units. However, for patients who have received an allogeneic hematopoietic stem cell transplant (HSCT), the choice of appropriate ABO group can be more difficult. This is particularly true in the case of ABO mismatch between the hematopoietic progenitor cell (HPC) donor and recipient. Although a blood group mismatch between donor and recipient ABO type does not seem to have any long-term drawbacks, providing appropriate transfusion support in the period after transplantation can be complex. These patients are known to require more transfusions due to delayed cellular engraftment and red cell aplasia. They are also at risk for acute and delayed red cell hemolysis from ABO incompatibility while engraftment takes place. Although some controversy exists, ABO-mismatched HSCT does not appear to adversely impact outcome or long-term survival in either pediatric or adult populations.

An ABO mismatch can lead to concerns during HSC infusion as well as post transplantation. In the setting of allogeneic transplantation, there are several possibilities for ABO antibody mismatch. When the donor possesses antibodies against recipient red cells, patients are deemed to have a minor mismatch. An example of a minor mismatch is when a patient (recipient) with group A red cells receives HPCs from a group O donor. A major mismatch is when the recipient has antibodies targeted to donor red cells. This would occur when a group O patient (recipient) receives HPCs from a group A donor. Finally, there is “two-way” incompatibility, where both major and minor mismatches occur, for example when a group A patient (recipient) receives HPCs from a group B donor. Table 50.1 summarizes both major and minor incompatibility by blood group. The key to successful transfusion for any of these mismatches is to reduce hemolysis during HPC infusion. For patients with a minor mismatch, this can be achieved by plasma reduction of the HPCs to significantly lower the amount of offending antibody. For patients with major mismatch, red cell depletion of the HSC product can be used to prevent acute hemolysis during infusion.

Antibodies can persist for weeks to months after transplantation, which can lead to ongoing issues in the selection of proper blood components. Patients can also present as chimeras after HSCT, with two distinct blood groups seen by routine blood typing. Fortunately, standardized strategies have been developed to provide the most compatible ABO components for these patients. For patients with major incompatibility from recipient anti-A or anti-B directed to donor red cells, recipient-type RBC units are necessary until ABO antibodies are no longer detected. For patients with minor incompatibility, recipient-type plasma and platelets should be used until the recipient’s red cells are no longer detected. Donor-type RBC units can be used immediately after HSCT for patients with minor incompatibility. Patients with two-way incompatibility require modified RBC units.
incompatibility require group O RBC units and group AB plasma and platelets until offending antibodies and cells are no longer detectable. Table 50.2 provides a transfusion protocol that can be followed for ABO-mismatched HSCT.\textsuperscript{10–12}

### Alloimmunization to red cell antigens

Despite significant immunosuppression, patients with malignancy can still mount immune responses to foreign red cell antigens, which can complicate transfusion and increase the risk for hemolysis.\textsuperscript{13,14} Rates for red cell alloimmunization in oncology patients have been most studied in patients with hematologic malignancies undergoing HSCT. These studies have shown that alloimmunization occurs in 2% to 8% of patients in these populations.\textsuperscript{15,16} Additional studies are needed to better assess the rate of red cell alloimmunization in patients with solid tumors or other oncologic conditions.

### Component modification: leukocyte reduction and irradiation

A major advance in blood component modification has been the implementation of prestorage leukocyte reduction techniques. Decreased numbers of white blood cells within transfusion components have been shown to reduce the risk of alloimmunization to human leukocyte antigens (HLA).\textsuperscript{17} In addition, leukocyte reduction can lower the rate of blood-borne transmission for pathogens that are carried within white cells, such as cytomegalovirus (CMV).\textsuperscript{18} According to the 2011 National Blood Collection Utilization Survey, approximately 85% of all red cell units in the United States were leukocyte reduced, most before storage.\textsuperscript{19}

Despite the use of leukocyte-reduced units, many oncology patients are still at risk for transfusion-associated graft–versus-host disease (TA-GVHD) because of their immunocompromised state. In cases of TA-GVHD, donor lymphocytes generate a profound immune response against the recipient’s cells.\textsuperscript{20} The underlying causes and manifestations of TA-GVHD are discussed in Chapter 60. Prevention of TA-GVHD can be accomplished by gamma irradiation of cellular blood components.\textsuperscript{21} Some within the field of transfusion medicine have argued for a policy of universal blood component irradiation, as the process has few side effects and may prevent cases of TA-GVHD in patients whose high-risk status is not known.\textsuperscript{22} However, the practicality and cost-effectiveness of such a policy have not been determined.\textsuperscript{22} The main disadvantage of irradiation is the induction of a potassium leak within the red cell membrane, thereby shortening the shelf of an RBC unit to no more than 28 days from the date of irradiation or the original expiration date, whichever comes first. There are no such concerns regarding the irradiation of platelets or plasma products, the latter of which does not require irradiation.

### Alternatives to allogeneic red cell transfusion

For oncology patients undergoing a surgical intervention, intraoperative blood recovery—a process where shed whole blood is centrifuged, washed of contaminants, and then reinfused—may be of benefit to reduce alloageneic blood usage.\textsuperscript{23} Although concern has been raised about the promotion of tumor cell metastasis with the use of such blood recovery in some cancer patients, several trials conducted in patients with hepatobiliary and genitourinary cancers have shown no evidence of decreased patient survival.\textsuperscript{24–26} Additional techniques including acute normovolemic hemodilution (ANH) and the use of preoperatively donated autologous whole blood can also be considered. However, these techniques are often not feasible in oncology patients who are too anemic and who can require surgery at unpredictable times. The lack of cost-effectiveness for preoperative autologous donation also limits its utility to oncology patients undergoing major surgery.\textsuperscript{27}

Another alternative to allogeneic red cell transfusion is the administration of erythropoietin-stimulating agents (ESAs). However, the chronic use of ESAs in patients with cancer and other critical illnesses has been found to have potential serious adverse effects. Several studies have found that ESA administration can lead to an increased risk for thrombosis.\textsuperscript{28} In addition, it has been postulated that erythropoetin may accelerate tumor growth and lead to decreased survival. Finally, studies have also shown that use of ESAs does not significantly decrease the need for allogeneic

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**Table 50.1 Compatibility by ABO Group in hematopoietic stem cell transplantation**

<table>
<thead>
<tr>
<th>Recipient ABO Group</th>
<th>O</th>
<th>A</th>
<th>B</th>
<th>AB</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>C</td>
<td>M</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>A</td>
<td>m</td>
<td>C</td>
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<td>M</td>
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<tr>
<td>B</td>
<td>m</td>
<td>mM</td>
<td>m</td>
<td>M</td>
</tr>
<tr>
<td>AB</td>
<td>m</td>
<td>m</td>
<td>m</td>
<td>C</td>
</tr>
</tbody>
</table>

C = compatible; M = major incompatibility; m = minor incompatibility; mM = both major and minor incompatibility (“two-way” incompatibility).

**Table 50.2 Transfusion protocol for HSCT patients**

<table>
<thead>
<tr>
<th>Recipient RBC type</th>
<th>Donor O RBC type</th>
<th>2nd choice PLT type</th>
<th>Donor A RBC type</th>
<th>2nd choice PLT type</th>
<th>Donor B RBC type</th>
<th>2nd choice PLT type</th>
<th>Donor AB RBC type</th>
<th>2nd choice PLT type</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>O</td>
<td>A or B</td>
<td>O</td>
<td>A</td>
<td>O</td>
<td>B</td>
<td>O</td>
<td>AB</td>
</tr>
<tr>
<td>A</td>
<td>A</td>
<td>O</td>
<td>A</td>
<td>A</td>
<td>O</td>
<td>AB</td>
<td>A</td>
<td>AB</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>O</td>
<td>AB</td>
<td>A</td>
<td>B</td>
<td>AB</td>
<td>AB</td>
<td>B</td>
</tr>
<tr>
<td>AB</td>
<td>AB</td>
<td>A</td>
<td>AB</td>
<td>A</td>
<td>AB</td>
<td>AB</td>
<td>A</td>
<td>or B</td>
</tr>
</tbody>
</table>

NOTE: Rh positive recipients with Rh negative donors receive Rh negative products. Rh negative recipients with Rh positive donors receive Rh positive products.
transfusion in critically ill patients. These findings led to a black box warning for the use of ESAs in the setting of cancer-related anemia.

**Platelet transfusion**

**Indications**

Platelet transfusion is intended to stop or prevent bleeding in thrombocytopenic patients. The use of platelet transfusion is a first-line therapy for acute hemorrhage in patients with thrombocytopenia or those receiving antiplatelet medication. However, some controversy exists over the use of platelet transfusion for bleeding prophylaxis. Initial studies that supported the use of platelets for bleeding prophylaxis arose from trials in leukemic patients who were noted to have decreased bleeding episodes after platelet transfusion. Later studies also demonstrated that prophylactic transfusion resulted in better outcomes and lower mortality compared to the use of therapeutic transfusion in patients with hematologic malignancy. In the early 1990s, the goal for routine bleeding prophylaxis was to keep platelet counts greater than 20,000/μL. However, more recent trials have shown that spontaneous hemorrhage is unlikely, even with platelet counts as low as 5,000 to 10,000/μL. In addition, patients transfused under more stringent criteria appear to have no change in morbidity and use significantly fewer blood products, thereby reducing the risks of chronic transfusion exposure.

Multiple clinical trials have shown that there is no increase in bleeding complications associated with the use of stringent platelet transfusion criteria. However, one retrospective study of patients after HSCT showed increased mortality in severely thrombocytopenic patients (platelet counts <10,000/μL), even though there was no increased risk of bleeding. Although difficult to completely interpret given the retrospective nature of the study, these data may imply a protective benefit from platelet transfusion other than bleeding prophylaxis in transplant patients. Prospective studies on survival and outcome that compare stringent and conservative approaches to platelet transfusion are still needed to determine the best course of treatment for thrombocytopenic oncology patients.

**Selection of ABO group and Rh type for platelet transfusion**

Platelets express ABO antigens, although interactions between these antigens and host antibodies do not usually mediate clinically significant transfusion reactions. Although type-specific platelets are preferred, most blood banks will transfuse ABO-mismatched platelets to adults without significant concern for incompatibility. However, the use of ABO-mismatched platelets in oncology patients can result in decreased therapeutic benefit or adverse reactions. For instance, a form of platelet refractoriness is mediated by ABO antibodies, with mismatched platelets cleared from circulation minutes to hours after infusion. Furthermore, there is some evidence to suggest that ABO incompatibility can promote the development of HLA alloimmunization in multitransfused patients. Another concern is the possibility that high-titer ABO antibodies in the plasma of donor platelets units may lead to hemolytic transfusion reactions in ABO-incompatible recipients. Children in particular may demonstrate clinically significant hemolysis to ABO-incompatible platelet transfusions owing to their small blood volume. Therefore, it is recommended that oncology patients with low platelet counts receive ABO-compatible platelet products when feasible. For populations undergoing HSCT, other considerations regarding major and minor mismatches are also relevant. Table 50.2 summarizes guidelines for platelet transfusion therapy in the peritransplant period.

Even though platelets lack Rh antigens, there remains a small concern for Rh alloimmunization during platelet transfusion due to the potential exposure to small numbers of residual red cells in the products collected from Rh-positive donors. Because of the immunogenicity of the D-antigen, even a few milliliters of red cells can lead to alloimmunization in Rh-negative recipients, yet the overall rate of alloimmunization is quite low. There is evidence to suggest that, in part due to immunosuppression, both adult and pediatric patients with hematologic malignancies are unlikely to form anti-D responses to Rh-incompatible platelet transfusions. Thus, the provision of Rh-incompatible platelet products is unlikely to cause D alloimmunization in oncology populations. This risk may be further reduced through the use of apheresis platelets, as these units have been shown to have fewer residual red cells. Nonetheless, it is still advisable to prevent Rh alloimmunization in children and females of childbearing potential because of the consequences of anti-D development in these populations. Alloimmunization can be prevented with a dose of 50 μg to 300 μg of Rh immunoglobulin (RhIg) provided within 72 hours of D antigen exposure. Care must be used to ensure that the intramuscular-only formulation of RhIg is never given intravenously.

**Selection of platelet products**

Historically, the majority of platelet products were derived from whole blood by centrifugation. These individual units were then pooled into groups of four to five to yield a product intended to raise platelet counts by approximately 50,000/μL. With advances in apheresis technology in the 1970s, an increasing number of platelet units were obtained from single donors that provided a platelet dose equivalent to the pooled product. The decision to use platelet pools versus platelets from individual donors relates to concerns about exposure to multiple donors, risk of alloimmunization, risk of adverse reactions, and platelet quality rather than increases in baseline platelet count as both products have similar viability and recovery. The risk for many of these issues are not specific to oncology and are discussed in greater detail in Chapters 18 and 20.

One particular concern for oncology patients is the possible increase in risk for platelet alloimmunization due to the large number of transfusions administered to these patients. This was a significant concern prior to the era of leukocyte reduction, especially for pooled platelet products. However, several studies, including the Trial to Reduce Alloimmunization to Platelets (TRAP), have demonstrated that the risk of alloimmunization is identical between leukoreduced pooled platelets and apheresis units. Once a patient has become alloimmunized, the use of platelet pools may be advantageous until crossmatch-compatible or HLA-matched units are available. In this scenario, an alloimmunized patient may be more likely to respond by chance to one of the four or five donors whose units constitute a platelet pool. Therefore, in alloimmunized patients, apheresis platelets should be used only if the unit is crossmatch-compatible or HLA-matched.

**Platelet refractoriness and alloimmunization**

Chronically transfused oncology patients often experience lower than expected platelet increments after transfusion, which is known as platelet refractoriness. This can be due to either immune or nonimmune causes. Platelet alloimmunization and refractoriness...
are discussed in detail in Chapter 18. In oncology patients, over 70% of cases of platelet refractoriness are due to nonimmunologic factors.50 Unfortunately, few clinical management options exist for patients with nonimmunologic platelet refractoriness. When possible, correcting the underlying cause (e.g., splenectomy for hypersplenism, removal of offending medications) can alleviate refractoriness. For the acutely bleeding patient or for hemorrhage prophylaxis, strategies of continuous platelet infusion (platelet drip) have been attempted with moderate success.53 The platelet drip, wherein a dose of platelet concentrate is infused slowly over a four-hour period, is intended to provide an ongoing source of platelets to maintain vascular integrity, while addressing the practical concern of blood bank platelet inventory management.

Although they constitute a minority of cases, the underlying cause of refractoriness in the remaining 20–30% of oncology patients is likely due to an antibody to a platelet antigen. Platelets express class I HLA and numerous other platelet-specific antigens. Human leukocyte antigens are the most common mediator of immunologic platelet refractoriness, although studies have shown that alloantibodies can develop to any platelet antigen.50,54 The treatment strategy for immune-mediated refractoriness is to provide antigen-negative components. Although often not a cause of true refractoriness, the first approach is to provide ABO-compatible units, which may lead to a more sustained increase in platelet count. The next option is to provide crossmatch-compatible platelets from the hospital blood bank or donor center. This involves crossmatching the patient’s serum with a variety of donor platelets and selecting units that do not cause agglutination.55 Crossmatch-compatible platelets have been proven to be as effective as HLA-matched platelets in raising platelet counts in alloimmunized patients.50,54,55 Thus, the decision to provide HLA-matched platelets should depend upon factors such as quality of the HLA match, severity of alloimmunization, and availability of crossmatched products. If a majority of tested donors are incompatible and HLA-matched products are needed, the recipient can be HLA typed to provide antigen-matched products.50,54 Polymorphisms of HLA class I antigens can complicate compatibility testing and make the process of finding fully matched donors difficult.

Unfortunately, once alloimmunization has occurred, immune modulation with corticosteroids, plasmapheresis, and intravenous immunoglobulin (IVIG) is of little benefit.56 Therefore, the overall best strategy to reduce immune-mediated platelet refractoriness is prevention of HLA and platelet antigen exposure. Leukocyte reduction has helped reduce the incidence of alloimmune platelet refractoriness by limiting exposure to HLA.17 Conservative transfusion strategies have also helped prevent exposure to HLA and platelet-specific antigens, and may play a role in reducing the frequency of alloimmunization.

**Component modification: irradiation, leukocyte reduction, and volume reduction**

As is the case with RBC units, platelets can be modified to maximize safety for oncology patients. Despite leukocyte reduction, platelet units contain small amounts of white cells. Thus, patients at risk for TA-GVHD should receive irradiated platelets.50 As mentioned previously, leukocyte reduction of platelet products helps reduce the rate of alloimmunization.17 According to the 2011 National Blood Collection and Utilization Survey, approximately 70% of all whole blood–derived platelet units were reported as leukocyte reduced.19 In addition, nearly all apheresis platelets are leukocyte reduced as part of the collection process.

Volume reduction of platelet products via centrifugation and resuspension in saline should be considered for oncology patients who have experienced severe allergic or anaphylactic reactions to platelet products.57 Volume reduction is also efficient at removing the plasma fraction of platelet products to reduce the risk of hemolysis associated with ABO-incompatible transfusion as well as the risk of volume overload.57

**Alternatives to platelet transfusion**

For patients unwilling to undergo platelet transfusion, or for severe platelet refractoriness, several medical therapies may be beneficial during bleeding episodes. A commonly prescribed drug, 1-deamino-8-D-arginine vasopressin (DDAVP or desmopressin), acts to stimulate the release of von Willebrand factor from endothelial cells, which can enhance platelet activity even at very low platelet counts.58 DDAVP is also of proven benefit for platelet dysfunction and bleeding associated with uremia.59 Antifibrinolytic therapies have also been employed as an adjunct to platelet transfusions for the bleeding patient. Medications such as aminocaproic acid, tranexamic acid, and apritinib have all been successfully used to reduce hemorrhage and alloimmune transfusion requirements in the bleeding patient.50,61

Chemical and cytokine-based stimulation of the marrow to endogenously increase platelet production has also been attempted. Agents such as thrombopoietin (TPO) and megakaryocyte growth factors have been synthesized, but clinical trials with some of these drugs led to the development of neutralizing antibodies and thrombocytopenia in some recipients.52,63 TPO and TPO-like growth factors are now used for some conditions such as immune thrombocytopenic purpura (ITP), and studies in oncology populations have been promising.64 Several agents, such as romiplostim and eltrombopag, have been licensed by the US Food and Drug Administration. Interleukin-11 (IL11), a cytokine that drives megakaryocyte production and division, has also been approved for use in thrombocytopenia.52,64

**Plasma and plasma-derived product transfusion**

**Indications for plasma transfusion and product selection**

The indications for transfusion of plasma and plasma-derived products, such as cryoprecipitated antihemophilic factor (AHF), is similar between oncology and other patient populations. For the majority of oncology patients, no additional consideration is given to the selection of ABO group for plasma or cryoprecipitate so long as the unit is ABO compatible with the recipient. Donor and recipient Rh types are not a consideration for infusion of plasma or cryoprecipitate. As mentioned in this chapter, for patients who have undergone allogeneic HSCT, the choice of ABO group can be complex and should be based upon consideration of major and minor mismatches. Table 50.2 summarizes guidelines for plasma transfusion therapy in the peritransplant period. The guidelines for cryoprecipitated AHF are identical to those for plasma. Because these products are acellular, there is no need for gamma irradiation, even in transplant and immunosuppressed oncology patients.

**Alternatives to plasma transfusion**

For some oncology patients, plasma transfusion may be contraindicated, may be ineffective, or may not provide rapid enough reversal of coagulopathic states. For these conditions, there are several alternatives to plasma products, consisting of concentrated...
or recombinant coagulation factors. Among the most commonly used agents for acute moderate to severe bleeding is recombinant activated factor VII, a potent activator of the coagulation cascade.65 Successful use of factor VIIa has been reported to help control massive bleeding in a variety of oncology patients.66–68 There is also a role for use of factor VIIa as a bypass agent for those oncology patients who acquire inhibitors to circulating coagulation factors, mainly factor VIII.69 However, factor VIIa failures in bleeding oncology patients have been reported for gastrointestinal bleeding and alveolar hemorrhage.70,71

The instances of factor VIIa usage cited above highlight the difficulty of recommending broad application of this therapy to the bleeding oncology patient. The most significant problem with making an evidence-based recommendation is that the vast majority of uses of factor VIIa in the literature are in the form of case reports. Few adequate clinical trials have been conducted to determine the safety and efficacy of this drug in oncology populations. Furthermore, appropriate dosing regimens are imprecise and mostly based on data gathered in trials performed in other critically ill patient populations. Factor VIIa also carries a number of risks, chief of which is the possibility for development of severe or even fatal arterial and venous thromboembolism.72 Thus, Factor VIIa may be considered as an alternative to plasma infusion, but should be used only after other interventions have failed.

**Intravenous immunoglobulin**

IVIG is used to provide passive immunity in highly immunosuppressed individuals and has also been used as an immunomodulatory therapy for patients with conditions such as immune thrombocytopenic purpura (ITP).73,74 For recipients of HPC products, IVIG has been associated with improved immune defense against pathogens such as CMV and has helped to decrease the complications of acute GVHD.75,76 The benefit of IVIG administration for chronic GVHD and infection prophylaxis in marrow transplantation is not clear and warrants further study.76

IVIG infusion is usually tolerated without significant adverse events in oncology patients. The common side effects include myalgia, headache, fever, and fatigue.77 A rare but serious complication of IVIG administration is acute renal failure seen with particular formulations that use sucrose as a globulin stabilizer.77 Thus, oncology patients with chronic renal insufficiency should be closely monitored during IVIG administration. Current IVIG products have not transmitted hepatitis B, hepatitis C, or human immunodeficiency virus, but there are rare case reports of transmission of parvovirus B19, a serious pathogen for oncology patients.78 Plasma is now screened for this virus before being pooled for fractionation.

**Granulocyte transfusion**

**Indications**

Historically, granulocyte infusions have been used in oncology patients with severe neutropenia to treat life-threatening, antibiotic refractory infections. The decision to initiate granulocyte transfusion usually represents failure of other forms of therapy. Only patients with a reasonable chance at sustained marrow recovery after resolution of the underlying infection are candidates for granulocyte products.79 It has been shown that humans should produce approximately 2–3 × 10^{11} polymorphonuclear cells daily to clear significant bacterial or fungal infections. For oncology patients whose marrow cannot support this level of production, doses of 1 × 10^{11} granulocytes per square meter of body area can be used to support the immunologic response.80

**Granulocyte donation and donor preparation**

A number of trials have been performed to evaluate the safety and efficacy of granulocyte transfusion using G-CSF stimulation in healthy donors. Several studies have suggested that granulocyte infusions from these donors are modestly effective for the treatment of bacterial and fungal infections.81 However, it has been hypothesized that improved outcomes may be seen with higher granulocyte doses. To obtain a larger number of granulocytes, the recently completed Safety and Effectiveness of Granulocyte Transfusion in Resolving Infection in People with Neutropenia (RING) study used G-CSF and dexamethasone to stimulate donors. Although this multicenter trial found that there was no difference in success rates between antibiotic and granulocyte therapies, only a small number of patients were enrolled.82

Healthy donors who qualify for granulocyte transfusion should be ABO-compatible with the intended recipient, and products must be crossmatched before infusion as granulocyte products may contain 6–12% red cells. A popular granulocyte mobilization regimen used in donors consists of the administration of 5 to 10 μg/kg G-CSF subcutaneously administered approximately 12 hours before leukapheresis.83 Historically, dexamethasone was also administered for granulocyte mobilization, but it is no longer routinely given. Granulocyte collections can be performed serially over 4–5 days to yield multiple doses for neutropenic patients. The side effects of granulocyte donation are usually mild and include bone pain, headache, fatigue, and fluid retention caused by G-CSF administration and apheresis.79,84,83

**Alloimmunization**

Alloimmunization is of significant concern given the large number of white cells, red cells, and platelets contained within a granulocyte product.85 In addition, patients previously alloimmunized to HLA often demonstrate a reduced response to granulocyte infusion.86 Thus, the expectation for successful response to granulocyte therapy should be tempered in an individual who has previously demonstrated HLA alloimmunization. If granulocyte transfusion is necessary for these patients, antigen matching for HLA may be required for an appropriate response to granulocyte transfusion.

**Granulocyte storage, component modification, and infusion**

Granulocytes must be stored at 20 to 24°C without agitation for a maximum of 24 hours from the time of collection.87 Because of the limited lifespan of neutrophils, it is preferred that granulocyte products be transfused within 6 to 8 hours of collection. Before issuance, the granulocyte products should be irradiated to prevent recipient TA-GVHD. Granulocytes should be infused through a 150–260-μm filter, but leukocyte reduction filters must never be used.88

**Adverse reactions to blood transfusion**

Oncology patients undergoing transfusion therapy are subject to the same set of adverse reactions as any patient receiving blood components. However, oncology patients are at increased risk for many types of adverse reactions. In addition, discerning between
an adverse transfusion event and exacerbation of an underlying condition can be difficult. Because they are often immunosuppressed, oncology patients are at increased risk for TA-GVHD (discussed in Chapter 60) and many transfusion-transmitted infections. In particular, CMV is one of the most problematic transfusion-transmitted infections for oncology patients. The virus is highly prevalent with a seroprevalence of 50–70% and has been found in the mononuclear cells of both seropositive and seronegative blood donors.89,90 Although CMV infections are rarely significant in immunocompetent hosts, infection can lead to severe pathology in immunosuppressed patients. These latter patients can develop CMV-related pneumonia, gastrointestinal inflammation, and delayed HSCT engraftment. Although CMV-seronegative blood can be obtained, availability is often limited due to the high seroprevalence in the general population. In addition, as noted above, even seronegative individuals can harbor infectious viral particles. Because CMV is present within mononuclear cells, the use of leukocyte reduction to prevent CMV transmission has also been employed. Several studies have found that leukocyte reduction is as effective as the use of seronegative units, but it does not completely eliminate the risk of CMV transmission.91,92 Thus, while the use of donor screening and leukocyte reduction is beneficial, oncology patients are still at some degree of risk for CMV exposure from blood transfusion.

**Adverse effects of hematopoietic progenitor cell infusion**

The majority of adverse events associated with HPC infusion are associated with the dimethyl sulfoxide (DMSO) content of the progenitor product. DMSO is a chemical modifier used in a majority of cryopreservatives that allows for the controlled freezing and thawing of mononuclear cells without development of membrane lysis.93 However, in vivo, DMSO is a toxic substance and has been linked to fever, nausea, vomiting, and chills during and immediately after HPC infusion. DMSO has also been linked to pulmonary and cardiovascular problems during HPC infusion, including dyspnea, hypotension, bradycardia, and arrhythmia.93,94 Due to the amount of DMSO infused, small children and those patients receiving multiple HPC units are more susceptible to DMSO-related problems.93 If the total infusion volume exceeds 10 mL/kg of recipient body weight, infusions are usually divided to reduce the risk of adverse reactions.

Researchers have also begun to evaluate whether HPC components other than DMSO can lead to infusion toxicity. Several recent studies have correlated adverse events to the numbers of granulocytes present in HPC products.95,96 These studies found that even after DMSO depletion, over half of patients undergoing HPC infusion experienced an adverse event such as fever, rigors, or dyspnea. It is therefore possible that the dyspnea associated with HPC infusion is not entirely caused by DMSO, but that granulocytes may contribute through transfusion-related acute lung injury (TRALI)-like mechanisms. These studies argue that a reduction in granulocyte content of the final HPC product would lead to fewer reactions. However, this is technologically challenging to achieve as removal of granulocytes would also remove the HPCs.

Bacterial contamination of HPC products can occur during collection or processing of the cells.97 Adequate field sterilization practices during stem collection and the processing of HPC products in sterile areas with air-controlled biosafety cabinets can reduce the risk of bacterial contamination.98 However, due to the significant handling of HPC products, contamination can be a frequent issue, particularly for marrow specimens.99 Because of this risk, units are routinely cultured and, if bacterially contaminated, provided to patients in conjunction with prophylactic, broad-spectrum antibiotics. Interestingly, one study has demonstrated that, of 33 patients who received bacterially contaminated HPCs, only six developed evidence of bacteremia and none had any long-term complications.100 Thus, bacterial contamination of an HPC product need not be an absolute barrier to infusion.

**Summary**

Transfusion support is a major therapy for many patients with hematologic and oncologic disorders. However, given their frequent exposure and often immunosuppressed state, they are often at more risk for adverse events due to transfusion. Compared to other patient populations, oncology patients are at increased risk for TA-GVHD, certain transfusion-transmitted diseases, alloimmunization to cellular antigens, and immunomodulation. In addition, HPC transplant patients present unique challenges to transfusion services, as they require specific assessment for potential ABO incompatibility. Careful selection of blood components and component modification is therefore necessary to provide appropriate therapy to these patients. Significant advances have been made in transfusion therapy, including more sensitive donor testing and blood component alternatives, which will continue to improve the safety of transfusion for oncology patients.

**Acknowledgments**

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A full reference list for this chapter is available at: [http://www.wiley.com/go/simon/ transfusion](http://www.wiley.com/go/simon/ transfusion)

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