Indications for RBC transfusions have been revised because patients can now be maintained at lower hemoglobin levels.


Transfusion Indications for Patients With Cancer
Thomas Watkins, DO, PhD, Maria Katarzyna Surowiecka, MD, and Jeffrey McCullough, MD

**Background:** During the last few years, considerable focus has been given to the management of anemia and coagulopathies. This article provides current concepts of red blood cell (RBC) and plasma coagulation factor replacements.

**Methods:** The literature was reviewed for clinical studies relevant to RBC transfusion indications and outcomes as well as for the uses of coagulation factor replacement products for coagulopathies most likely encountered in patients with cancer.

**Results:** Most patients without complications can be treated with a hemoglobin level of 7 g/dL as an indication for RBC transfusion. However, the effects of disease among patients with cancer may cause fatigue, so transfusions at higher hemoglobin levels may be clinically helpful. Leukoreduced RBCs are recommended as standard therapy for all patients with cancer, most of whom do not develop coagulopathy. Transfusions to correct mild abnormalities are not indicated in this patient population. Data are inconclusive regarding the value of coagulation factor replacement for invasive procedures when the international normalized ratio is below 2.

**Conclusions:** Indications for RBC transfusion have become more conservative as data and experience have shown that patients can be safely and effectively maintained at lower hemoglobin levels. Coagulation factor replacement is unnecessary for most modest coagulopathies.

**Introduction**
Transfusion is an important part of cancer therapy. Red blood cells (RBCs) may be needed because of myelosuppression for chemotherapy or anemia in the setting of chronic disease. Because of myelosuppression, platelets are often part of the continuum of care for patients with cancer. Typically, plasma is not needed because coagulopathy is not a major aspect of cancer or its therapy. However, in infrequent situations in which coagulation factor replacement is needed, plasma can be vital to the treatment of patients with cancer. Most infections can be managed with antimicrobials; however, granulocyte transfusions may sometimes be considered for recalcitrant infections in patients with neutropenia. The uses and indications for all of these blood components have undergone changes over the last few years. This report is a summary of those changes and the current clinical indications and uses of RBCs, plasma, and granulocytes.

**Transfusions**
RBC transfusion is common in the treatment of patients with cancer. Overall, patients with oncological and...
hematological malignancies use around 34% of the RBC supply. In patients with cancer, as is similar with any other patient population, the indication for RBC transfusion is to alleviate symptomatic anemia. The decision to transfuse should not be driven by the hemoglobin concentration, and no single criterion can be used as an indication for RBC transfusion. Thus, the patient’s clinical status should be of utmost consideration.

Anemia may occur in 90% of patients during chemotherapy and, furthermore, cancer treatments often cause the loss, destruction, and decreased production of RBCs — all of which lead to anemia. In particular, lung and gynecological cancers are associated with anemia because the treatments for such cancers include platinum-based therapies. Anemia in cancer may decrease quality of life and increase cancer-induced fatigue. Cancer-associated anemia may also be an indicator of poor clinical outcomes. If urgent correction of anemia is unnecessary, then erythropoietin treatment may be a valid alternative to RBC transfusion and can decrease RBC transfusion rates.

In general, RBC transfusions are used to treat (1) tissue hypoxia due to inadequate RBC mass, (2) acute anemia due to trauma or surgical blood loss, (3) anemia in patients receiving chemotherapy, and (4) cardiovascular decompensation of chronic anemia. They are also used to ensure the optimal tissue oxygenation in patients with anemia undergoing radiation therapy. RBC transfusion is not indicated for the correction of anemia due to iron deficiency, as a source of nutritional supplementation, or in volume expansion.

Dynamic physiological changes in patients with anemia help allow the decreased RBC mass to continue to oxygenate tissue. In brief, these changes include increased blood flow (as blood viscosity decreases) and increased oxygen offloading in hypoxic tissues (as the concentration of 2,3-diphosphoglycerate increases in the RBCs). In the setting of anemia, the overall blood volume is maintained with increased plasma volume. Compensatory cardiac output changes maintain adequate perfusion. As a result of these dynamic physiological changes, symptoms of anemia rarely manifest until hemoglobin values significantly dip. Animal studies indicate that extreme hemodilution can be tolerated in healthy animals. One study showed that 6 of 7 baboons survived hematocrit levels down to 4% and that they maintained adequate cardiac compensation at hematocrit levels as low as 10%. In addition, humans can tolerate very low levels of hemoglobin.

RBC transfusions have been used for decades; recently, the effectiveness of RBC transfusions has been evaluated in randomized trials so that the best evidence can be ascertained to guide transfusion decisions. In some patient populations, nontransfused patients have better outcomes than transfused patients and patients who receive fewer units do better than those who receive more RBC units. The following clinical trials described below illustrate this concept.

Results from a trial by Hébert et al changed the practice of transfusion. This study was a randomized controlled trial that compared a "liberal" transfusion strategy (defined as a post-transfusion goal of a hemoglobin concentration between 10 and 12 g/dL with a transfusion indication of a hemoglobin concentration of 10 g/dL) with a "restrictive" transfusion strategy (defined as a post-transfusion hemoglobin concentration between 7 and 9 g/dL with a transfusion indication of a hemoglobin concentration of 7 g/dL). The trial included 838 volunteers and demonstrated an overall in-hospital mortality rate significantly lower in the participants who received the restrictive transfusion. The 30-day mortality rates were not significantly different between 2 groups. However, clinically “less ill” volunteers (Acute Physiology and Chronic Health Evaluation score < 20) or those who were younger (< 55 years of age) had significantly lower 30-day mortality rates than those who were “more severely ill” or older following the restrictive transfusion strategy. Thus, the study results demonstrated that a restrictive transfusion strategy is at least equivalent to a liberal transfusion strategy in all groups, except among those with severe ischemic heart disease, and the restrictive transfusion strategy was potentially better in “less ill” and younger people. This was the first well-structured clinical trial of RBC transfusion suggesting that maintaining patients at lower hemoglobin levels might be beneficial.

Vincent et al evaluated the 28-day mortality rate of 3,534 patients from 146 western European intensive care units (ICUs). The mortality rates among study volunteers were 22.7% and 17.1% among those receiving transfusions and those not receiving transfusions, respectively. The study controlled for patients with a similar degree of organ dysfunction. The receipt of an RBC transfusion in the ICU increased a patient’s odds of dying by a factor of 1.37.

Corwin et al analyzed anemia and blood transfusions among 4,892 study volunteers who were critically ill in US ICUs. The study results showed that the number of RBC transfusions was an independent predictor of longer ICU stay, longer length of hospital stay, and increased mortality rates.

In another trial, Carson et al compared the effect of a transfusion threshold of 10 g/dL with 8 g/dL in cardiovascular patients undergoing surgical hip fracture repair. The trial involved 2,016 patients older than 50 years of age, and the primary outcome was death or the inability to walk across a room without human assistance on 60-day follow-up. Rates of death or an inability to independently walk after 60 days, in-hospital morbidity rates, and in-hospital complications were similar in the 2 groups. Thus, the
liberal transfusion strategy did provide clinical benefit over the restrictive (9 g/dL) strategy.

Evidence does not support a benefit to a post-transfusion hemoglobin concentration above 10 g/dL. However, this level may be helpful in pediatric patients with cancer who have acute blood loss or cyanotic heart disease due to the additional challenges of this patient population.

Despite well-performed clinical trials, no universal RBC transfusion criterion exists. A restrictive transfusion strategy is at least equivalent to a liberal transfusion strategy in the majority of clinical scenarios. However, in clinical practice, the underlying condition of the patient and his or her transfusion goals and desired outcomes should be considered. RBC transfusion may be indicated in a patient with symptoms of anemia and a hemoglobin level below 7 g/dL. Transfusion with hemoglobin concentrations between 7 and 10 g/dL may be indicated when significant underlying comorbidities exist, such as cardiac disease, respiratory disease, bone marrow failure, or other hematological diseases; this is because anemia may not be well tolerated in these patients. Traditionally, single unit transfusions were not recommended; however, as the hemoglobin indication has decreased and transfusion has become more conservative, it has become clear that the transfusion of 1 unit can be effective and sufficient. Single unit vs 2-unit transfusions can reduce blood use as much as 25% with no adverse clinical consequences. Specifically, the AABB (formerly American Association of Blood Banks) recommends transfusion at a hemoglobin concentration of 7 to 8 g/dL for hospitalized patients who are stable, 8 g/dL for those with cardiovascular disease, and higher hemoglobin (unspecified) concentrations for patients with acute coronary syndromes.

Reactions or adverse events due to RBC transfusion are uncommon and may occur in 1% to 3% of transfusions. The most common adverse event is febrile nonhemolytic transfusion reaction, which typically is due to human leukocyte antigen (HLA) antibodies in the recipient or an allergic reaction to plasma proteins. The most severe yet rare reaction is acute hemolysis, usually due to ABO incompatibility due to administration error. Because the changes that occur during RBC storage have become better understood, concern has developed as to whether RBCs nearing the end of the routine 42-day storage might have undergone changes, thus making them risky for certain patients. The focus of research has been on patients with cardiovascular disease or those undergoing surgery; presently, however, no data suggest this is a concern for patients with malignancy. For more information, please refer to the article by Drs Qu and Triulzi in this issue.

RBC transfusion has an immune-modulating effect. RBC transfusion may be associated with increased risks of postoperative infections, longer durations of hospital stay, and longer stays in the ICU. RBC transfusion has also been linked to longer durations of mechanical ventilation, increased incidences of multiple organ failures, and an overall increase in health care costs. However, these issues have not been resolved. In the previous few years, concerns have been raised that RBC transfusions might exacerbate cancer; however, no consensus has yet to be made on this issue. For more information about this topic, please read the article by Drs Dasararaju and Marques in this issue.

The rationale for the transfusion of RBCs is to increase the delivery of oxygen to the tissues, but physiological changes with RBC storage may limit this goal. In addition, the ability of transfused RBCs to deliver oxygen to areas most in need of oxygenation may be decreased. The physiological changes that occur in stored RBCs (collectively called the RBC storage lesion) may limit, to some degree, the ability of the transfused RBCs to enter the microcirculation and may decrease vasodilation by altering the bioavailability of nitric oxide. During storage, RBCs undergo changes that result in their removal from the circulation within 24 hours of transfusion. However, some RBCs recover biochemical normalcy and survive normally. Other changes to stored RBCs include microparticle formation, changes in shape, decreased concentration of RBC 2,3-diphosphoglycerate, decreased pH, and the decreased availability of adenosine triphosphate and glucose. In combination, the physiological changes resulting from the RBC storage lesion may limit the delivery of oxygen by the transfused RBCs. However, no consensus exists on whether RBCs stored for long periods of time are deleterious to any patient group; thus, RBCs of any storage age can be used for patients with cancer. Leukoreduced RBCs have decreased rates of transfusion reactions, HLA alloimmunization, and have the potential benefit of modifying the transfusion-related immune modulation (TRIM) effect (if it exists). Thus, leukoreduced RBCs are recommended as the standard blood product for routine use in patients with cancer.

Frequent transfusions for cancer and chemotherapy treatments over an extended period of time may result in iron overload. Treatment regimens for many solid organ cancers avoid this complication because the transfusion-dependent period is shorter in duration due to chemotherapy and irradiation regimens. As transfusion dependence increases during treatment, the risk of transfusion-transmitted infection, allergic response, and severe transfusion reactions increase with each unit transfused. Health care professionals must weigh any benefit from RBC transfusions against these risks.
Special Red Blood Cell Products
Patients with cancer may require specially prepared RBC products due to frequent comorbidities.

Leukoreduced Blood Components
The leukocyte content of different blood products widely varies (as high as $1 \times 10^9$ in whole blood to $<0.6 \times 10^6$ in fresh frozen plasma [FFP]). Leukoreduced blood products are blood products produced by filtration or apheresis to decrease the number of leukocytes remaining in the product to below $5 \times 10^6$ leukocytes/component. Leukoreduced blood components are beneficial in 3 ways: (1) decreased frequency of febrile nonhemolytic transfusion reactions, (2) decreased HLA sensitization of recipients, and (3) decreased likelihood of cytomegalovirus (CMV) transmission via transfusion.

Leukoreduction may significantly reduce febrile nonhemolytic transfusion reactions and may decrease cardiopulmonary transfusion reactions (transfusion-related acute lung injury and transfusion-associated circulatory overload). Presumably, this occurs through reduced levels of bioactive lipids and soluble CD40L in leukoreduced RBCs, which would have been produced by leukocytes had they remained in the blood product. As the RBCs age in storage media, they develop well-established changes that include decreased deformability and decreased levels of adenine triphosphate and 2,3 diphosphoglycerate. Donor leukocytes release cytokines and lipid mediators capable of affecting neutrophils in a time-dependent course during RBC storage. Prestorage leukoreduction decreases the release of metabolites and cellular components into the RBC product.

Leukoreduction may also be effective in decreasing alloimmunization and platelet transfusion refractoriness. This is especially relevant to patients with cancer as they may receive numerous RBC and platelet transfusions during their treatment cycle. A study published in 1997 examined 1,047 patients with acute myeloid leukemia. Those who received leukoreduced platelets had decreased levels of lymphocytotoxic antibodies and lower rates of refractoriness to platelet transfusion when compared with the study controls who received unmodified pooled platelet concentrates.

Leukoreduction may decrease the TRIM effect of blood transfusion that may lead to possible increased cancer recurrence. Evidence suggesting that blood transfusion may decrease immune function was established more than 30 years ago, showing that survival rates were increased following renal transplantation. Other, more controversial data exist regarding RBC transfusion and tumor recurrence perioperatively. Vamvakas and Carven showed that patients with colorectal cancer who received RBC transfusion perioperatively had longer lengths of hospital stays when adjusted for multiple confounding factors related to the severity of their illness, difficulty of operation, and risks for postoperative infections. In addition, Blachman reported adverse effects on tumor recurrence in 50% of nonrandomized trials. Further data suggest that an immunomodulatory role in transfusion is related to a dose-dependent association (ie, increased RBC transfusion) with postoperative bacterial infections and RBC transfusion.

Cytomegalovirus Infection and Safe Blood Components
Transfusion-transmitted CMV is a possible risk for severe infectious complications in severely immunosuppressed patients with cancer who have not been previously infected with CMV. Donor screening questionnaires cannot exclude CMV seropositive volunteers, and CMV has a high seroprevalence; 40% to 50% of adults have CMV antibodies. Furthermore, regional blood centers may have difficulty obtaining CMV negative products locally because the majority of adults in these areas may be CMV seropositive. An additional issue with CMV seronegative donors is that some may still carry CMV in their leukocytes or plasma. For transfusion recipients who are immunologically competent, CMV infection is not life threatening. However, CMV infection in immunocompromised patients with cancer can result in potentially fatal sequelae, including delayed hematopoietic stem cell engraftment, pneumonia, and severe gastrointestinal inflammation. However, even in these patients the risk is low. By using CMV-safe leukocyte blood cells, one study found that CMV infection was reduced from 2.4% to 1.3% and CMV disease was reduced from 2.4% to 0%.

CMV is leukotropic and is not present in the RBCs, platelets, or plasma of healthy donors. Leukoreduction decreases the likelihood of CMV transmission, and leukoreduced products are generally regarded as being safe from CMV infection and equivalent to CMV antibody negative blood.

Irradiated Blood Components
A serious and typically fatal complication of blood transfusion is transfusion-associated graft-vs-host disease (TA-GVHD). The transfusion of viable allogeneic T-lymphocytes in blood products to an immunosuppressed individual has the potential for TA-GVHD, a complication that can be prevented by irradiating the blood components. The actual incidence of TA-GVHD is low in most patients with cancer, and the irradiation of blood products is indicated in few, small, but well-defined populations of patients at risk. The types of patients who require irradiated cellular blood products include neonates, patients with congenital immune deficiencies.
(eg, severe combined immunodeficiency syndrome, Wiskott–Aldrich syndrome), those with a hematological malignancy who are undergoing chemotherapy, and recipients of allogeneic and autologous bone marrow transplantations, partial HLA-matched products (often directed donations from genetic relatives), and all granulocyte products. Patients with HIV/AIDS and patients with solid organ tumors do not require irradiated RBCs.\(^{37}\)

Leukoreduction does not prevent TA-GVHD. Although patients with suppressed immune systems are at the most risk for TA-GVHD than any other patient group, rare instances exist in which transfusion between similar HLA-type individuals has resulted in TA-GVHD in immune-competent individuals. These include situations in which the donor and recipient share an HLA haplotype such that the patient does not recognize the donor cells as foreign and, thus, does not eliminate them, creating the potential for TA-GVHD.\(^{48,49}\)

**Washed Red Blood Cells**

The indications for washed RBC products in patients with cancer are largely in line with the requirements for washed products in general medical settings. Overall, the goal for washing RBC products is to decrease plasma elements, including antibodies, plasma proteins, and electrolytes, that may have adverse effects on the recipient. Patients with severe immunoglobulin A deficiency have the potential to have anaphylactic transfusion reactions. Washing RBCs removes immunoglobulin A from the unit. Rarely, patients who experience recurrent febrile nonhemolytic and urticarial transfusion reactions may also benefit from washed RBCs. Additional indications for washed RBCs may include rapid or large volume (> 25 mL/kg) transfusions in small volume or in patients with small stature.

Washed products may be indicated for transfused products following irradiation, because some patients with cancer and poor renal function may have difficulty with the increased extracellular potassium in RBCs after the irradiation.

Some patients with cancer may also require volume-reduced RBC products. If a patient with cancer has a compromised renal or circulatory system that cannot accommodate the increased volume of the transfused RBC unit, then volume reduction may be indicated.

**Fresh Frozen Plasma**

FFP is plasma that has been separated from whole blood or obtained by plasmapheresis and frozen at \(-0.4^\circ\mathrm{F} \approx -18^\circ\mathrm{C}\) or below within 8 hours of collection. At this temperature, FFP can be stored for up to 12 months after donation. A unit of FFP has a volume of about 200 to 250 mL and contains all of the coagulation proteins present in whole blood. FFP does not contain RBCs and, thus, can be administered without regard for the Rhesus (Rh) type of the patient. However, because plasma contains antibodies, it should be ABO matched to avoid possible hemolysis. Additional plasma preparations used clinically include plasma frozen within 24 hours of collection (FP24), which contains reduced levels of labile coagulation factors V and VIII. FP24 is frequently used by blood banks interchangeably with FFP when a clinical need exists for fibrinogen replacement.

FFP transfusions are typically undertaken in the setting of bleeding or in preparation for an invasive procedure when laboratory coagulation screening test results are abnormal.\(^{50,51}\) These are typically defined as prothrombin and partial thromboplastin times greater than 1.5 times the normal limit. The usual dose of FFP is 10 to 15 mL/kg body weight, but the dose may be higher in the setting of massive blood loss. This dose would be 3 to 4 units of FFP; however, in practice most health care professionals use 2 units and, thus, patients are often underdosed. A dose should be given at least every 6 hours until hemostasis is achieved or coagulation parameters are stabilized.\(^{51}\) The need for additional FFP is based on the replenition of factor VII, which has the shortest half-life of all the coagulation factors. If FFP is given for bleeding, then its effectiveness can be best assessed by monitoring the clinical response of the patient. If it is given to correct abnormal coagulation parameters, then the parameters may be followed as an indication of hemostasis response.\(^{50}\)

If the patient is also receiving platelets, then it is important to remember that when platelets are stored in plasma, every plateletpheresis unit contains the equivalent of 1 bag of FFP. In this situation, either smaller doses or no additional doses of FFP may be required. In Europe and the United States, platelets may be stored in an additive solution of electrolytes instead of plasma.\(^{52}\) Because the additive solutions replace plasma, those platelet products cannot be considered a source of coagulation factors.

National guidelines for the use of FFP exist both in the United States and abroad.\(^{50,51}\) The clinical indications for the therapeutic use of FFP include active bleeding before an invasive procedure in the presence of an inherited or acquired clotting factor deficiency, active bleeding in the setting of a consumptive coagulopathy or disseminated intravascular coagulation, massive transfusion, immediate reversal of warfarin effect in an actively bleeding patient, and thrombotic thrombocytopenic purpura.\(^{53}\) Patients with cancer may be at risk for abnormalities of hemostasis due to tumor pathology and evolution of the disease as well as treatment effect. Coagulation factor abnormalities may occur as a result of vitamin K deficiency from malnutrition, diarrhea, liver disease, biliary obstruct-
tion, use of vitamin K antagonists, and antibiotic therapy.61 In the setting of abnormal coagulation screening test results, invasive procedures such as surgery, line placement, indwelling catheter placement, among others, may result in significant blood loss. The use of FFP along with vitamin K and cryoprecipitate for additional fibrinogen replacement may be considered in these situations.

However, the effectiveness of FFP used prophylactically in the nonbleeding patient prior to an invasive procedure or surgery in the setting of abnormal coagulation values has not been proven.62 A paucity of good randomized controlled trials have compared the use of FFP with no FFP. Two well-conducted randomized controlled trials reported a lack of evidence for the prophylactic use of FFP.55

Several issues exist when considering the use of FFP. Reversing a coagulopathy with FFP generally requires a large volume of transfused product. This could be a significant concern, particularly for patients who have blood volume status issues prior to transfusion and who are at risk for transfusion-associated volume overload. In addition, due to the relatively low concentration of clotting factors in a unit of FFP, the increase in factor activity after more than 1 L of transfused FFP may be modest. If immediate correction of coagulopathy is needed, then a product containing factors II, VII, IX, and X and proteins C and S and more concentrated forms of coagulation factors should be considered.

The transfusion of plasma carries significant risk that should be weighed against its perceived benefit, especially when FFP is prophylactically used. Potential serious complications include transfusion-associated lung injury and volume overload as well as transfusion-transmitted infection. Allergic reactions to plasma are common and may, in rare cases, be life threatening.

Pathogen inactivation is a process by which blood components are treated in a manner that damages nucleic acids, thus rendering the components free of infectious pathogens.63 One of these plasma components, Octaplas (Octapharma USA, Hoboken, New Jersey), is available for use in the United States. Octaplas is prepared from pools of about 1,000 donor units and then subjected to solvent detergent treatment for pathogen inactivation and reallocated into units of about 200 mL, which is similar to a standard unit of FFP.64 The solvent detergent treatment spares coagulation factors so that the product is considered to be similar to FFP.

**Granulocyte Transfusion**

Infections — particularly fungal infections — continue to be a source of morbidity and mortality in patients with neutropenia because of aggressive chemotherapy or hematopoietic stem cell transplantation. With a granulocyte count below 1,000, the risk of infection is increased, and this risk is even further increased based on the duration of neutropenia. During the 1970s, several studies established that granulocyte transfusion was associated with improved survival rates in patients with gram-negative sepsis and granulocytopenia for at least 10 days.65-67 No carefully controlled studies of granulocyte transfusion exist in other clinical settings. However, as our ability to manage neutropenia and to treat gram-positive and gram-negative sepsis has improved with the use of newer antibiotics, the value of granulocyte transfusions has become questionable.68 Granulocyte transfusions in the 1970s up to the present contained about $1 \times 10^{10}$ granulocytes and were obtained from donors, most of whom were stimulated with dexamethasone. The advent of granulocyte colony-stimulating factor (G-CSF) and its resultant use in patients to increase granulocyte counts and mobilize hematopoietic stem cells led to the possibility of using G-CSF stimulation of blood donors in order to obtain larger numbers of granulocytes for transfusion. When it is combined with dexamethasone, G-CSF can result in granulocyte counts of up to 40,000/µL with a yield of up to $8 \times 10^{10}$ granulocytes.69 Small studies of these transfusions have suggested efficacy.65-66 However, no studies adequately establish the clinical value of granulocyte transfusions. A multicenter trial managed by the National Marrow Donor Program in 5 US centers studied 40 patients with infection and neutropenia.67 Survival rates with complete or partial response rates 4 weeks after initiating transfusions were 38% for invasive mold infection, 40% for bacteremia/candidemia, and 60% for severe bacterial infection.67 Thus, evidence suggests that granulocyte transfusion therapy is feasible and may be clinically effective. A recently completed large, multicenter clinical trial did not show benefit from granulocyte transfusions except in a small subgroup of patients who received very high doses of granulocytes.68 These result suggest it is possible that granulocyte transfusions may be clinically beneficial if very high doses of cells are given.68 Currently, if granulocyte transfusions are to be used, then cells obtained from dexamethasone and G-CSF–stimulated donors are recommended to obtain a substantial number of cells. These transfusions can provide an increased granulocyte count to more than 5,000/µL in many patients,66 and subsequent transfusions can maintain counts in this range.67 Indications for considering granulocyte transfusion include bacterial of fungal infections of the blood or proven tissue infections of bacteria of fungi unresponsive to antibiotics. Response to transfusion should not be evaluated on a daily basis, but granulocyte transfusions should be considered as a course of therapy similar to antibiotics. Therefore,
transfusions should be continued for a minimum of 5 days or until the infection has been resolved.

Granulocytes should be transfused as soon as possible after collection because storage time is limited.\textsuperscript{69-71} Transfusion of a unit of granulocytes should not take more than 2 hours. Reactions to granulocyte transfusions are relatively common and generally similar to a febrile nonhemolytic transfusion reaction. Severe pulmonary reactions have been reported when granulocytes were infused in close proximity to amphotericin, but whether this represents a major risk or applies to other antifungals is not clear. It is best to separate the transfusion of granulocytes from amphotericin infusion by at least 2 hours.

**Outpatient Transfusion**

With improvements in medical treatments and longer survival rates among patients with cancer, the management of anemia and thrombocytopenia on an outpatient basis has become an important consideration. In patients with acute myeloid leukemia or high-risk myelodysplastic syndromes, the availability of highly effective antimicrobials and transfusion support has allowed a shift in care from inpatient to outpatient settings.\textsuperscript{72} In these patient populations, outpatient management of cytopenias has been shown to be safe and effective in both the postconsolidation and postinduction therapy periods.\textsuperscript{73-74}

Outpatient treatment has several potential benefits, including reduced cost and resource utilization, improved quality of life, and decreased incidence of nosocomial infections.\textsuperscript{75} Important factors involved in outpatient management include establishing therapy guidelines, determining the location where the therapy takes place, and patient education. Communication with the local blood bank is also important, particularly with regard to special products.

Indications and guidelines for inpatient transfusion are well established. However, it is not clear whether these should be applied or modified for outpatient transfusion. Thus, because no national guidelines exist for outpatient transfusions, each institution must determine its own indications.

On one hand, the rational and physiology of the management of anemia or thrombocytopenia are the same for inpatients or outpatients, and, thus, possibly the guidelines and indications for transfusion should be the same. By contrast, patients are living in a different environment as outpatients. They are less acutely ill, less fragile, and more stable and thus should be more resilient. However, they are more removed from easy and quick access to medical care. Their care is provided by intermittent outpatient clinic visits that may involve travel and inconvenience. Thus, it is appropriate to manage transfusion to provide the stability and continuity that enables the patient to function in the outpatient setting. It might also be appropriate to transfuse larger-than-usual inpatient doses of the component if doing so extends the time to the next clinic visit. For example, larger doses of platelets extend the time to the next transfusion,\textsuperscript{76,77} and, if the sole reason for a patient to return for a clinic visit is for a platelet count to determine the need for the next transfusion, then a larger dose can extend the time for the next clinic visit. Doing so provides a better quality of life for the patient and may also be more cost effective, although no such studies have been done to determine whether this is true.

Another consideration is the laboratory value as the indication for the transfusion. For instance, if the hemoglobin level is slightly above 7 g/dL and the hospital’s guideline for RBC transfusion is 7 g/dL, then the transfusion might be considered to be inappropriate in the quality system monitoring. By contrast, if a return clinic visit is not needed for 1 or 2 weeks, then it would be inappropriate to have the patient return sooner simply to repeat the hemoglobin level to determine when the hemoglobin concentration is less than 7 g/dL so the transfusion would meet the hospital guideline. It seems that more appropriate care would be to transfuse the patient at that visit despite a hemoglobin concentration above the level recommended by the guideline. Thus, transfusing 2 units of RBCs or transfusing at a hemoglobin concentration of 8 g/dL or even 9 g/dL could be considered appropriate in the outpatient setting.

The topic of indications for outpatient transfusions is not established and deserves considerable analysis and discussion because of different patient life situations. We also need to determine ways in which to offer the most cost-effective methods for providing care in the outpatient setting.

**Conclusions**

A hemoglobin level of 7 g/dL is a suitable indication for red blood cell transfusion in stable patients without complications. However, patients with cardiovascular disease or acute coronary syndrome should be transfused at a hemoglobin level of 8 g/dL. Indications for transfusion in patients with other types of complications have not been established. Patients with cancer have reported an increased feeling of wellbeing and stamina when maintained at hemoglobin levels at about 7 g/dL, but no structured studies have determined the optimal hemoglobin levels for patients with advanced cancer.

Although coagulopathy is uncommon in patients with cancer, fresh frozen plasma is used as replacement therapy for moderate to severe coagulopathy. Fresh frozen plasma may also be used for increases in the international normalized ratio in preparation for invasive procedures, although no structured studies
have established the exact value.

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