

New York State Council on Human Blood and Transfusion Services

***A PHYSICIAN'S GUIDE TO
TRANSFUSION OPTIONS***

Second Edition
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INTRODUCTION AND OVERVIEW

The mission of the New York State Council on Human Blood and Transfusion Services is to set standards and develop recommendations for the use of transfusion-related products and services in New York State. This document is intended to assist in discussions with patients regarding decisions about the need for transfusion and the options available to meet such needs. Intrinsic to these discussions is an understanding of the current indications for the transfusion of different blood components; the current safety of the community blood supply; and the various options available in addition to allogeneic transfusion, including strategies to reduce or even avoid the use of blood products.

CURRENT RECOMMENDATIONS FOR THE TRANSFUSION OF BLOOD COMPONENTS

Table 1 summarizes the most frequently used blood components and provides information on their indications and precautions. Tables 2, 3, and 4 list indications for administration of red blood cells (RBCs), plasma [fresh frozen plasma (FFP), 24-hour plasma] and platelets, respectively, and also note some situations when blood components are not or are rarely indicated. For additional information, see the Council's various guidelines, available at: www.wadsworth.org.labcert/blood_tissue/blood_services_guideline.htm.

Generally accepted indications for transfusion of red cells in various clinical settings have been the subject of several publications in recent years. In the nonsurgical setting, the decision to transfuse red cells is based upon the severity of anemia, duration of anemia, availability of alternate therapies, the patient's symptoms, and the presence of co-morbidities that would either increase or decrease the risk of significant hypoxia at a given hemoglobin concentration (see Table 2).

In the setting of surgery, trauma, or other instances of acute blood loss, the indications for administration of red blood cells are influenced by the severity of anemia, the presence of other clinical conditions, and the rate of hemorrhage. Estimated blood volume loss, clinical signs and symptoms, and hemoglobin concentration measurements are standard methods for assessing transfusion needs in acutely bleeding patients. It should be noted that these approaches carry limitations because anesthetic agents may mask some signs and symptoms of anemia, assessment of the amount of blood lost can be difficult, and hemoglobin measurements are usually artifactually low in patients who have received large volumes of fluids that temporarily expand plasma volume.

It is accepted that, in many clinical situations, selected patients can be satisfactorily managed by using a variety of blood-sparing strategies instead of transfusion. Much of this information is derived from experience with patients who have religious objections to transfusion. In the event that transfusion of blood components is likely necessary, the following information is intended to assist clinicians and patients in deciding among the various options available.

ALLOGENEIC BLOOD AND COMPONENTS (COMMUNITY)

New York State regulations mandate multiple donor screening steps and procedures to minimize the risk of infectious disease transmission. All allogeneic blood donors must complete a questionnaire to ensure that, on the day of donation, they are in good health and have no known medical condition that would pose a risk to the blood recipients or to themselves during the donation. In particular, donors are closely questioned about possible risk factors for HIV infection, hepatitis and other infectious diseases believed to be transmissible by blood transfusion. Finally, donors are told how to confidentially inform the blood collection organization of information that may render their donated blood unsuitable, if they fail to declare a risk factor at the time of donation or develop an illness following donation.

Allogeneic blood donors are tested for a variety of infectious disease markers, including hepatitis B surface antigen (HBsAg); HIV-1, hepatitis C virus (HCV), and West Nile virus (WNV) nucleic acid; antibodies to hepatitis B core antigen (anti-HBc), HCV, HIV-1, HIV-2, and human T-cell lymphotropic virus types I and II (HTLV-I/II); syphilis; and Chagas disease. When new tests become available for donor testing, they are implemented as indicated.

Despite all the above precautions and testing, blood components continue to pose a small risk of transmission of pathogens, including viruses, bacteria, and parasites. These risks have been estimated by means of various statistical tools. Table 5 lists known infectious disease risks and provides some estimates of current risks. Currently unrecognized pathogens may also emerge in time. Some studies have suggested that transfusion of allogeneic blood results in an immunomodulatory effect that may predispose transfused patients to infection and other complications.

Prior to transfusion, the hospital transfusion service ascertains that the component is of the appropriate blood group for compatibility with the patient, and performs any compatibility testing indicated. Testing determines whether the patient possesses any red cell antibodies that might react with the blood component being administered and decrease the effectiveness of the transfusion, or increase the likelihood of a transfusion reaction. If such clinically significant antibodies are identified, antigen-negative units are selected.

DIRECTED BLOOD DONATIONS

Some patients may wish to meet their transfusion needs with blood donated by relatives or friends. It is important for such patients to recognize that there is no evidence that such donations are any safer than those from volunteer community donors. In fact, some concern has been voiced that they may be statistically less safe.

Directed donors may feel such pressure to help the patient that they may give inaccurate information about their state of health. Furthermore, most directed donors are first-time donors in whom the risk of disease is higher than traditional repeat donors. Therefore, directed blood donations appear to be no safer than community allogeneic donations in terms of infectious disease and immunomodulatory risks. Transfusion of blood from close relatives also may increase the risk of transfusion-associated graft-versus-host disease, which is a rare, but serious and often fatal, complication. To avoid this risk, directed donor cellular blood components must undergo irradiation prior to transfusion. On rare occasions, the use of blood from close relatives may be absolutely contraindicated, including transfusion of patients who may undergo possible future bone marrow transplantation. Finally, in the case of a woman with child-bearing potential, donations from her husband/partner may be contraindicated

because the woman could become immunized to an antigen the father might share with a future fetus.

Directed donations of blood and components are permitted in New York State. While opportunities for directed donation of whole blood are plentiful, donation of platelets or plasma may be difficult to arrange, and must be coordinated with the expected date of transfusion and blood collection center procedures.

AUTOGENEIC DONATION AND TRANSFUSION

In an attempt to avoid exposure to allogeneic blood and blood components, the option of presurgical autogeneic donations and/or perioperative red cell recovery may be considered. Whether one or more of these options is appropriate for the patient is determined by the health of the patient, the feasibility of collection, and the ability to predict the needs of the patient during surgery.

For autogeneic blood collection by blood centers, patient-donors must undergo the same tests as for community donations. Such testing should be performed a maximum of 30 days prior to the date of collection. The ordering physician and the patient are informed if an autogeneic patient-donor is positive on any of the standard tests. Authorization for release of such units to the hospital may be needed from the patient's attending physician and from the hospital's transfusion service director. Once a unit is found to be positive for any of the infectious disease tests, some collection agencies may consider the patient to be ineligible for further autogeneic donations. Testing of the donated unit is not required by regulation if collection is performed by a hospital for use in that hospital, but transfusion service policies of individual hospitals may require such testing. Blood recovered and transfused as part of perioperative autogeneic cell recovery procedures does not require testing.

Pre-Surgical Autogeneic Blood Deposit

Following discussion with the patient, the physician must request this service by completing and submitting a physician order form that is usually required by blood centers prior to scheduling the first donation appointment. To ensure proper labeling of the autogeneic unit, the order form must include: patient's full legal name (as used during the hospitalization); a unit identification number; date of birth; date of anticipated transfusion; name and address of the hospital where the surgery will be performed; and name, address, and telephone number of the ordering physician.

Autogeneic patient-donors need not meet the standard eligibility guidelines set for community donors; however, certain criteria should be met. Patients with infectious diseases, such as HIV infection or AIDS, may be ineligible for autogeneic deposit at some blood collection facilities, and some hospitals may not accept such units if collected. A hemoglobin concentration of at least 11 g/dL prior to each donation is required, unless otherwise approved by the medical director of the blood collection facility. To prevent patients from becoming anemic as a result of the procedure, oral iron supplements are generally recommended for patients depositing more than one unit.

In addition, the patient-donor's physician must disclose any significant patient medical history that may affect the safety of the donation process or suitability of the unit for the patient, and must certify that, in the physician's judgment, the patient may safely undergo phlebotomy. Particular attention should be accorded to a history of atherosclerotic heart

disease (e.g., angina, myocardial infarction, bypass surgery); cardiac valvular disease (e.g., aortic stenosis); cerebrovascular disease (e.g., stroke); seizure disorder, especially if not well-controlled by medication; and any medical condition in which rapid loss of 500 mL of blood, or a prolonged vasovagal reaction, might pose a risk. Autogeneic blood deposit is contraindicated in patients with active infection/bacteremia or a condition that predisposes to bacteremia (e.g., having a urinary catheter or any skin-penetrating device).

Special arrangements with the blood bank may be required for patient-donors under 16 years of age. A parent or legal guardian must accompany the patient-donor. For autogeneic patient-donors weighing less than 110 pounds (50 kg), it may be possible to collect a volume smaller than a full unit at a given sitting.

At the donation site, the patient-donor must complete a medical history questionnaire, and undergo assessment of temperature, blood pressure, pulse, and hemoglobin concentration. Should any of these values fall outside of autogeneic donation criteria, the patient is deemed ineligible for donation at that visit. The entire process requires about an hour; the donation itself, about ten minutes.

Autogeneic patient-donors may generally give blood as frequently as twice per week during the six-week period preceding the anticipated transfusion date. The last deposit may be made no later than three working days before the anticipated surgery. (Note: If blood needs to be shipped outside New York State, the last donation generally needs to be made no later than ten working days before its anticipated use).

Depending on the preservative solution used, red blood cells can be stored in liquid form from 21 to 42 days. The most commonly used solution allows liquid red cells to be stored for 42 days. If surgery is postponed, frozen storage may be available under certain conditions. Under limited circumstances, autogeneic platelet, plasma, and cryoprecipitate donations may be arranged with selected blood centers on a case-by-case basis.

The cost effectiveness of autogeneic procedures has been increasingly called into question, given the additional costs involved in preoperative deposit of autogeneic red cell units (as many as 55 percent of these are eventually discarded rather than used), the risk of rendering the patient anemic and more likely to be transfused as a result of the procedure, combined with the improved safety of allogeneic blood transfusions and the availability of other more convenient and less costly options. Furthermore, predonated autogeneic blood holds the same risk of error as allogeneic blood, carries a risk of bacterial contamination that may exceed that of allogeneic blood, and is subject to the same detrimental effects of refrigerated storage outside of the body, which can reduce the effectiveness of the transfusion. For these reasons, this approach is most effective when there is a high expectation that the blood will be transfused; or in exceptional circumstances, such as patients with multiple red blood cell antibodies or rare blood groups, and patients who do not consent to allogeneic transfusion but accept presurgically deposited autogeneic blood. This procedure is not usually accepted by people with religious objections to transfusion.

PREOPERATIVE ASSESSMENT AND PLANNING

Advance planning is essential to minimizing transfusion requirements in the perioperative period. Accurate history taking and physical examination, with special attention to existing anemia and bleeding disorders, are critical. Careful evaluation of pre-existing anemia and its treatment prior to surgery are an effective strategy for reducing surgical transfusion

requirements. The use of anticoagulants and antiplatelet drugs should be carefully re-assessed before and after surgery to minimize their effect on bleeding, while maintaining their needed function. Whenever possible, agents that could adversely affect coagulation in the perioperative period (e.g., aspirin and medications containing aspirin, antiplatelet agents and anticoagulants) should be discontinued or replaced for the seven days prior to the surgery, in consultation with prescribing physicians.

Perioperative Autogeneic Transfusion

For many patients, collection of autogeneic blood in the perioperative period, using intraoperative or postoperative blood recovery techniques, or via isovolemic hemodilution, is a safe transfusion alternative. It can be considered for procedures anticipated to result in large blood loss, following trauma, and for patients who may require a volume of blood not sufficiently provided by autogeneic donation prior to surgery.

Perioperative blood recovery consists of collection and reinfusion of blood lost during and immediately after surgery. The most likely candidates for intraoperative recovery are patients in whom substantial blood loss is anticipated, such as those undergoing cardiac, vascular, orthopedic, neurosurgical, or gynecological procedures. Intraoperative collection may be contraindicated if the operative field contains hypotonic fluids, or is grossly contaminated with bacteria, as with spilled intestinal contents, or by malignant cells. In cases of malignancy, the use of leukoreduction filters has been proposed to minimize the likelihood of hematogenous dissemination of malignant cells. The theoretical risk of metastatic cell seeding must be weighed against the potential benefit of blood recovery in a particular patient.

Blood recovered intraoperatively may be transfused directly after collection (unwashed) using a disposable system, or may be processed (washed and concentrated) prior to infusion using a semi-automated cell washer. Blood recovered without processing must be reinfused within six hours of the start of collection. Blood recovered with processing and stored at room temperature must be reinfused within four hours of the completion of processing, while blood processed and refrigerated may be reinfused within 24 hours of the start of collection, provided that refrigerated storage was initiated within four hours of the completion of processing. A 40-micron filter should be used for reinfusion. In addition, in the case of Cesarean section, consideration should be given to the use of a filter intended to remove fetal squamous cells and other particulates. Because recovered blood is likely to contain fetal red blood cells, consideration should be given to blood group incompatibilities and administration of Rh immune globulin, if indicated.

The oxygen-carrying capacity of recovered red blood cells equals or exceeds that of stored allogeneic red cells; the cell survival is comparable. While reinfusion of unwashed recovered blood is less complex and less costly, such blood has a low hematocrit and may contain procoagulants and contaminants. For this reason, hospital policy may limit the quantity of collected blood that may be reinfused without washing. Methods that include processing are more complex, requiring specialized equipment and specially trained staff.

Postoperative blood recovery is performed during the immediate postoperative period. While blood can be collected from surgical drains through a variety of devices, filtered through a 40-micron filter, and then returned to the patient, the safety of reinfusing unwashed orthopedic wound drainage and mediastinal drainage has been questioned. In particular, concerns regarding infusion of fat, fibrin degradation products, activated coagulation factors and complement have been raised. Furthermore, the amount of red cells recovered from

orthopedic drainage is so limited that many experts consider the risks to outweigh the benefits. The use of a device designed to concentrate and wash recovered blood is preferred if large volumes are to be reinfused. Blood collected postoperatively must be reinfused within six hours from the start of collection.

Isovolemic hemodilution consists of withdrawal of blood from the patient at the beginning of a surgical procedure and its reinfusion at the end. A minimum of two to three units of blood must be collected for the procedure to be effective. The patient's blood volume is maintained isovolemically with crystalloid or, preferably, colloid solutions. Hemodilution reduces red cell loss by lowering the hematocrit of the blood lost during surgery. In addition, the autogeneic units contain viable platelets and coagulation factors. Careful management of the fluid balance and monitoring of the patient's cardiac status are essential during this procedure. Low preoperative hemoglobin, infection, coagulopathy, and significant cardiac, pulmonary, renal or hepatic disease rank among the concerns and relative contraindications. Blood collected for isovolemic hemodilution and stored at room temperature must be reinfused within eight hours of the start of collection, while blood stored refrigerated may be reinfused within 24 hours of the start of collection, provided that refrigerated storage was initiated within eight hours of the start of collection. This procedure is most effective in cases in which the anticipated surgical blood loss equals or exceeds 1,500 mL (generally 30 percent of the patient's estimated blood volume). The feasibility of any of these options may depend on the surgery being performed, hospital policies and procedures, and the availability of necessary staff and equipment.

REDUCING BLOOD LOSS

A simple, yet effective, measure to reduce blood loss is to minimize phlebotomy for diagnostic procedures. Both the phlebotomy frequency and volume of blood drawn should be minimized, for example, by using pediatric-sized blood tubes for adults. In addition to reliance on conservative indications for transfusion and transfusion "triggers" the use of local absorbable and systemic hemostatic agents (desmopressin and anti-fibrinolytic drugs) may reduce bleeding. Careful monitoring of the patient's temperature and blood pH may help maintain hemostatic function. Finally, in selected situations, bleeding may be reduced significantly by deliberate induction of mild hypotension, careful surgical technique, and, in spinal surgery, appropriate positioning of the patient to avoid inferior vena cava compression with resultant engorgement of the epidural plexus.

Additional guidance on blood conservation options may be found in New York State Council on Human Blood and Transfusion Services documents entitled, *Guidelines for Physician Options for Blood Conservation* and *Considerations for Patients with Religious Objections to Transfusion*, available at: www.wadsworth.org/labcert/blood_tissue/blood_physician.shtml, and www.wadsworth.org/labcert/blood_tissue/objections.htm, respectively.

PERTINENT LITERATURE

American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: An updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. *Anesthesiology* 2006;105:198-208.

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Table 1. Summary of Blood Components, Their Indications, and Applicable Precautions

Component	Indications	Action	Not Indicated	Precautions	Hazards
Red Blood Cells	Symptomatic anemia	Restores oxygen-carrying capacity	Pharmacologically treatable anemia	Must be ABO compatible	Infectious disease; sepsis; allergic reactions; acute lung injury; circulatory overload
Fresh Frozen Plasma and 24-Hour Plasma	Deficit of labile and/or stable coagulation factors; TTP; severe deficit of protein S Note: Coagulation protein content varies by plasma type.	Replaces labile and/or stable factors	Simple volume replacement	Should be ABO compatible	As above
Cryoprecipitate	Hypofibrinogenemia; selected platelet dysfunctions, including renal failure and selected cases of von Willebrand disease; factor XIII deficiency; may be used as part of fibrin glue	Provides fibrinogen, factor XIII, and vWF	Other coagulation abnormalities		Infectious disease; sepsis; allergic reactions; acute lung injury
Platelets and Platelets by Apheresis	Bleeding due to thrombocytopenia or platelet dysfunction; prophylaxis in patients with < 30 - 50,000/ μ L prior to an invasive procedure or with < 5 - 10,000/ μ L	Provides viable platelets with normal function; restores primary hemostasis	Thrombocytopenia due to platelet destruction (ITP, TTP) in the absence of severe bleeding	As above	As above; alloimmunization to HLA and platelet antigens
Granulocytes	Severe neutropenia (< 500 PMN/ μ L) with sepsis	Provides viable granulocytes	Infections responsive to antibiotics alone	Must be ABO compatible; do not use a leukoreduction filter	As above

For more information, see the Council's blood services guidelines, available at: www.wadsworth.org/labcert/blood_tissue/blood_services_guidelines.htm.

Table 2. General Guidelines for Transfusion of Red Blood Cells in Acute Blood Loss

<p>Blood loss of:</p> <ul style="list-style-type: none">• 15-30 percent of blood volume (800-1500 mL in an adult) – should be treated with crystalloids or colloids. No need for transfusion unless patient has preexisting anemia, limited cardiopulmonary reserve, or ongoing blood loss.• 30-40 percent of blood volume (1500-2000 mL in an adult) – requires rapid volume replacement with crystalloids or colloids. Red blood cell transfusion is probably needed.• > 40 percent of blood volume (> 2000 mL in an adult) – requires rapid volume replacement, including red blood cells.
<p>Hemoglobin (Hb) concentration:</p> <ul style="list-style-type: none">• Hb \geq 10 g/dL – transfusion is rarely indicated.• Hb 6-10 g/dL – indications for transfusion should be based on the patient's risk of inadequate oxygenation from ongoing bleeding and/or high-risk factors, such as age, cardiovascular compromise, or respiratory disease.• Hb \leq 6 g/dL – transfusion is almost always indicated.

For more information, see *Guidelines for Transfusion of Red Blood Cells – Adults* (available at: www.wadsworth.org/labcert/blood_tissue/redblood.htm).

Table 3. Indications for Transfusion of Plasma (Fresh Frozen Plasma and/or 24-Hour Plasma)

- Prophylaxis associated with invasive procedures in nonbleeding patients with acquired coagulation defects
- Emergency surgery in nonbleeding patients on warfarin with a prothrombin time (PT) greater than 1.5 times the mean of the reference range, whenever time does not permit warfarin-induced factor deficiency reversal with vitamin K
- Prophylaxis in nonbleeding patients with known hereditary coagulation abnormalities
- Bleeding patients with acquired multiple coagulation deficiencies, including those developed prior to or during massive transfusion
- Bleeding patients with known, hereditary coagulation factor deficiencies for which specific clotting factor concentrates are not available
- Thrombotic thrombocytopenic purpura (TTP) or other thrombotic microangiopathy (e.g., hemolytic uremic syndrome or HELLP syndrome)
- Rare indications
 - a. Factor XIII deficiency, as an alternative to cryoprecipitate
 - b. Prophylactic or therapeutic replacement of anticoagulant proteins (e.g., antithrombin, protein C, protein S), whenever specific clotting factor concentrates are not available. Patients with severe protein S deficiency require fresh frozen plasma (FFP) for replacement.
 - c. C1 esterase inhibitor deficiency (e.g., life-threatening hereditary angioedema), whenever specific factor concentrates are not available.

FFP and other types of plasma are NOT indicated:

- For patients with abnormal coagulation test results due to clotting factor deficiencies for which specific clotting factor concentrates are available, patients with coagulation factor inhibitors, or for heparin reversal
- For volume expansion
- As a nutritional supplement or protein source
- Prophylactically, following cardiopulmonary bypass
- To promote wound healing
- For patients with hypoglobulinemia

For more information, see *Guidelines for the Administration of Plasma* (available at: www.wadsworth.org/labcert/blood_tissue/plasma.htm).

Table 4. Indications for Transfusion of Platelets

- Prophylaxis in patients with platelet counts < 30,000 - 50,000/ μ L prior to an invasive procedure. A platelet count > 100,000/ μ L is recommended for neurosurgical and ophthalmologic procedures.
- Active microvascular bleeding attributed to platelet dysfunction or thrombocytopenia. In surgical and obstetric patients, usually indicated when the platelet count is <50,000/ μ L in the presence of excessive bleeding.
- Intrinsic or acquired platelet dysfunction prior to an invasive procedure
- Prophylaxis in patients with severe thrombocytopenia
 - a. < 5,000/ μ L – likely indicated
 - b. > 5,000 - < 20,000/ μ L – requires clinical judgment based on bleeding risk

Platelet transfusion is rarely indicated:

- In surgical or obstetric patients with normal platelet function and a platelet count >100,000/ μ L.
- For vaginal deliveries or operative procedures with limited anticipated blood loss.
- Prophylactically, following transfusion of a fixed number of RBC units.
- When thrombocytopenia is due to increased platelet destruction (e.g., heparin-induced thrombocytopenia, idiopathic thrombocytopenic purpura, thrombotic thrombocytopenic purpura).

For more information, see *Guidelines for the Administration of Platelets* (available at: www.wadsworth.org/labcert/blood_tissue/platelets.htm).

Table 5. Infectious Disease Risks of Blood Transfusion

Primary Risks in Immunocompetent Recipients

- Bacterial contamination (Gram-negative bacteria)
- Hepatitis B
- Hepatitis C
- HIV-1

Additional Risks in Immunocompromised Recipients

- Cytomegalovirus
- Bacterial contamination (Gram-positive bacteria)
- Parvovirus B19
- Epstein-Barr virus
- Babesiosis (*Babesia microti*)

Very Rare Risks

- Chagas disease (*Trypanosoma cruzi*)
- Malaria (primarily *Plasmodium malariae* and *P. falciparum*)
- West Nile virus
- Hepatitis A
- Syphilis (*Treponema pallidum*)
- Variant Creutzfeldt-Jakob disease
- HIV-2
- Human T-cell lymphotropic viruses
- Leishmaniasis (visceral *Leishmania tropica* and possibly *L. donovani*)
- Human anaplasmosis (formerly human granulocytic anaplasmosis and human granulocytic ehrlichiosis)
- Dengue fever

Theoretical, But Unreported Risks

- Creutzfeldt-Jakob disease
- Human ehrlichiosis (formerly human monocytic ehrlichiosis)
- Lyme disease (*Borrelia burgdorferi*)
- Toxoplasmosis (*Toxoplasma gondii*)

Estimated Residual Risks of Some Transfusion-transmissible Viruses

Virus	Recent Risk Estimate Ranges
HIV-1	1/1,525,000 – 1/2,300,000 units
HCV	1/1,390,000 – 1/1,800,000 units
HBV	1/344,000 – 1/144,000 units
HTLV	1/1,208,000 units

For more information, see *Guidelines for Evaluation of Transfusion-associated Infections* (available at: www.wadsworth.org/labcert/blood_tissue/infect.htm).