

Blood Transfusion



A six-word narrative about living with blood cancer from patients in our LLS Community

Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith, nutrition and optimism. Finding the joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.



Discover what thousands already have at
www.LLS.org/Community

Join our online social network for people who are living with or supporting someone who has a blood cancer. Members will find

- Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff
- Accurate and cutting-edge disease updates
- The opportunity to participate in surveys that will help improve care.

Inside This Guide

2 Introduction

3 Blood Donation

4 The Blood

7 Preparing Blood Components

Pooled Platelets

Pheresis Platelets

8 Safety of Blood Transfusions

Autologous and Directed Donations

Donor Screening and Collection

Testing for Carriers of
Infectious Disease

Removing White Cells

11 Transfusions for Patients with Blood Cancer

Red Cells and Platelets

White Cells

Transfusion of Red Cells

Iron Overload

Transfusion of Platelets

Transfusion of Granulocytes

Transfusion of Plasma and
Cryoprecipitate

Use of Intravenous Gamma Globulin
(IVIG)

Transfusion of Albumin

Palliative Care and Transfusions

16 Complications of Blood Transfusions

Reactions That Damage or Destroy
Red Cells

Reactions That Cause Fever

Reactions That Cause Hives

The Patient Makes Antibodies to the
Donor's Blood

Transmission of Viral Infections

Transmission of Cytomegalovirus
(CMV)

Transmission of Bacterial Infections

Graft-Versus-Host Disease (GVHD)

Effect on a Patient's Immune System

20 Resources and Information

23 References

Acknowledgement

The Leukemia & Lymphoma Society gratefully acknowledges, for their critical review and important contributions to the material presented in this publication,

Joanna Heal, MBBS, MRCP

and

Neil Blumberg, MD

*Professor of Pathology and Laboratory Medicine Director of Clinical Laboratories
Director of the Transfusion Medicine Unit, Blood Bank, and Stem Cell Storage Facility
University of Rochester Medical Center, Rochester, New York*

Introduction

Each year more than 15 million units of whole blood are collected and 5 million patients are transfused with blood components in the United States. (Source: The 2011 National Blood Collection and Utilization Survey Report; 2011 is the most recent year for which data are available.) Each unit is generally divided into three components: red cells, platelets and plasma. Most of the red cells are transfused to patients undergoing surgical procedures. Patients with leukemia, lymphoma, myeloma, myelodysplastic syndromes and myeloproliferative neoplasms (blood cancers) frequently receive platelets and some red cells; they may require more blood components overall than surgical patients because their need is likely to continue over a period of weeks or longer. In addition, most patients who undergo marrow or blood stem cell transplantation will be transfused.

The most frequently asked questions about blood transfusion relate to

- The safety of the blood supply (see page 8)
- Diseases that can be transmitted by blood components (see page 9)
- Other complications that may occur following blood transfusion and what is being done to reduce those risks (see page 16).

New treatments may have been approved since this book was printed. Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Feedback. Visit www.LLS.org/publicationfeedback to give suggestions about this booklet.

Blood Donation

The need for blood transfusions for patients with blood cancers never takes a holiday. Every day thousands of blood components are transfused to patients. Blood cannot be made artificially; thus, patients' lives literally depend on volunteers who give blood on a regular basis. Volunteers have the option to donate platelets alone versus donating whole blood. As the population gets older and more sophisticated medical practices are developed, the need for blood component therapy will grow. In many areas of the country, blood centers have had difficulty keeping up with the need, and as a result there have been frequent shortages.

About 60 percent of the US population is eligible to donate blood. People in good health, at least 17 years old and weighing at least 110 pounds can donate blood every two months. Family members and friends often ask what they can do to help support their loved one during his or her illness. One relatively easy and simple thing that eligible people can do is to donate blood, and encourage friends and family members to donate. Often, blood centers are able to send a card to the patient after a donation is made, to acknowledge the donor's gift in the patient's name. While there should be no pressure to donate, this is one altruistic and valuable contribution to the care of patients and costs the donor no money. The gift of blood donation supports all patients and families dealing with blood cancers or other diseases, for which transfusions may be an essential part of treatment, and ensures that blood will be available when it is needed.

The Blood

The blood is the main transport system in the body. It carries raw materials and finished products from where they originate to where they are used and transports waste products to disposal sites. Some of the contents of the blood are traveling to a specific destination. For example, sugar (glucose) may be going from the liver to muscle to provide a source of energy for movement; coagulation factors may be carried from the liver to a cut blood vessel to ensure clotting. Integral parts of the blood are the red cells, different types of white cells and platelets. Red cells and platelets perform their functions and spend their mature existence entirely within the blood.

The blood accounts for about 7 percent of the body weight of a normal adult. This means that a 154-pound person (70-kilogram) has about 10 pints (5 liters) of blood. Smaller adults and children have proportionately smaller blood volumes.

Blood is composed of plasma and cells suspended in plasma (red cells, platelets and white cells [neutrophils, monocytes, eosinophils, basophils and lymphocytes]). Plasma is largely made up of water in which many chemicals are dissolved. These chemicals include

- Proteins
 - Albumin, the most common protein in blood
 - Blood-clotting proteins, made by the liver
 - Erythropoietin, a protein made by the kidneys that stimulates red cell production
 - Immunoglobulins, antibodies made by plasma cells in response to infections including those we develop from our vaccinations (such as poliovirus antibodies, which are made by normal plasma cells in the bone marrow)
- Hormones (such as thyroid hormone and cortisol)
- Minerals (such as iron and magnesium)
- Vitamins (such as folate and vitamin B₁₂)
- Electrolytes (such as calcium, potassium and sodium).

Red Cells. The red cells make up a little less than half the volume of the blood. They are specialized cells that are composed of a disc-like envelope that contains the red-colored protein hemoglobin, which gives the blood its characteristic color. Hemoglobin picks up oxygen in the lungs and delivers it to the cells all around the body, and then picks up carbon dioxide from the body's cells and delivers it back to the lungs, where it is removed when we exhale. The normal red cell lives for 120 days in circulation, and so about 1 percent of the body's red cells (about half an ounce) must be replaced by the bone marrow each day.

The red cell membrane is composed of protein, fats and carbohydrate molecules that are associated with the various blood groups. The ABO blood group (the four principal types are A, B, AB, and O) was described in 1900 and the Rh blood group in 1945. Transfused red cells should match the patient's ABO and Rh blood groups. Many other blood group antigens (foreign substances that stimulate an immune response in the body) have since been described. However, these are not usually matched for transfusion unless the patient has developed antibodies to these antigens as a result of previous pregnancies or blood transfusions.

Platelets. The platelets are small cells (one-tenth the size of red cells) that help stop bleeding at the site of an injury. They are present in high concentration in the blood and circulate for only about 10 days. That means that 10 percent of them are replaced each day to maintain the platelet count at normal levels. Platelets function in two ways. When a person has a cut, the vessels that carry blood are torn open. Platelets stick to the torn surface of the vessel, clump together and plug up the bleeding site with the help of blood-clotting proteins such as fibrin and electrolytes such as calcium. Later, a firm clot forms. The vessel wall then heals at the site of the clot and returns to its normal state. The second function of platelets is to provide a surface that promotes blood clotting. Recent research suggests that platelets are an important part of the immune system and contribute to inflammation and blood clotting (thrombosis).

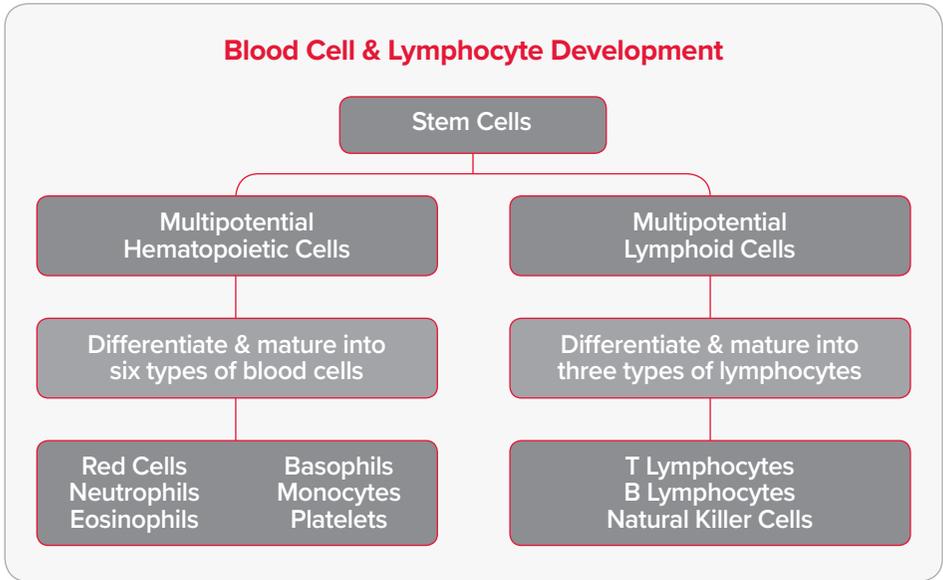
White Cells. The white cells include neutrophils, eosinophils, basophils, monocytes and lymphocytes.

Neutrophils and monocytes are called “phagocytes” (eating cells) because they can ingest bacteria or fungi and kill them. Unlike the red cells and platelets, the monocytes can leave the blood and enter the tissue, where they can attack the invading organisms and help combat infection. The neutrophils survive for short periods, less than a day or two, and thus must be replaced quickly by new cells delivered from the marrow. Eosinophils and basophils are white cells that participate in allergic reactions.

Lymphocytes are a key part of the immune system. There are three major types of lymphocytes: T lymphocytes (T cells), B lymphocytes (B cells) and natural killer (NK) cells. They make up a complex immune system that responds to foreign organisms and helps fight cancer. Most of the lymphocytes are found in the lymph nodes, the spleen, a few other lymphatic organs and the lymphatic channels, but some enter the blood. They move from one lymphatic organ to another by means of the lymphatic channels and the circulation. About one billion new lymphocytes are made each day.

Plasma. The plasma is the liquid portion of blood in which blood cells are suspended. It is composed primarily of water, in which many chemicals and gases are dissolved. In addition, there are minerals, carbohydrates, fats, vitamins, hormones and enzymes. Plasma contains coagulation factors and gamma

globulin, which contains antibodies. Coagulation factors can be removed from plasma and manufactured into concentrated products to treat patients with coagulation factor deficiencies, such as hemophilia. Gamma globulin can also be concentrated from plasma and is used to help people who lack the immunoglobulins that fight infection.



Stem cells develop into blood cells (hematopoiesis) and lymphocytic cells.

Bone Marrow. Marrow is a spongy tissue where blood cell development takes place. It occupies the central cavity of bones. In newborns, all bones have active marrow. By the time a person reaches young adulthood, the bones of the hands, feet, arms and legs no longer have functioning marrow. The spine (vertebrae), hip and shoulder bones, ribs, breastbone and skull contain the marrow that makes blood cells in adults. The process of blood cell formation is called “hematopoiesis.” A small group of cells, the stem cells, develop into all the blood cells in the marrow by the process of differentiation (see figure above).

In healthy individuals there are enough stem cells to keep producing new blood cells continuously. Blood passes through the marrow and picks up the fully developed and functional red and white cells and platelets for circulation in the blood.

Some stem cells enter the blood and circulate. They are present in such small numbers that they cannot be counted or identified by standard blood count tests. Their presence in the blood is important because they can be collected by a special technique. There are also methods to induce more stem cells to leave their home in the marrow and circulate in the blood, allowing a greater stem cell collection to occur. If enough stem cells are harvested from a compatible donor, they can be transplanted into a recipient.

Stem cell circulation, from marrow to blood and back, also occurs in the fetus. After birth, placental and umbilical cord blood can be collected, stored and used as a source of stem cells for transplantation.

Preparing Blood Components

More than 98 percent of the blood supply in the United States comes from volunteer donors. Most donors give a single unit of whole blood at a site convenient to their work or home.

The availability of plastic bags that can have one or more satellite bags attached in a completely sterile system allows for flexibility in preparing the donated blood. The use of plastic bags allows the blood center to make a variety of different blood products. Usually three or four blood components, such as red cells, platelets, plasma and cryoprecipitate are prepared from each unit of whole blood donated.

“Cryoprecipitate” is the name for the blood component obtained by freezing plasma and then thawing it at 4°C. It is used to provide certain clotting factors for people who need them due to a genetic or acquired clotting defect. The usefulness of component therapy is that each patient is given only the specific component that he or she needs. This allows one donation to benefit up to four patients and conserves precious blood resources.

Each component has to be prepared within a certain time from collection and stored at a specific temperature and for a specific length of time to maintain optimum function. The primary blood bag contains an anticoagulant that prevents the blood from clotting after it has been collected. This unit is spun gently in the lab using a centrifuge, so that the heavier red cells settle at the bottom of the bag. The lighter plasma, which contains the platelets, can then be siphoned off into one of the attached satellite bags. A red cell storage solution is then added to the red cells, the tubing is sealed and the red cells are separated from the other bags. A red cell unit is about 250 milliliters (about 10 ounces) and is stored at 4°C for 42 days. Ideally, the red cells transfused should be the same ABO and Rh group as the patient's. Certain exceptions are made in emergencies.

The bag containing the platelet-rich plasma is then centrifuged at a higher speed to deposit the platelets at the bottom of the bag along with about 50 milliliters (about two ounces) of plasma. Most of the plasma is siphoned into a third attached bag. The unit of platelets is sealed and separated, leaving a bag of plasma. Platelets need to be stored in an incubator at room temperature and rocked gently. They have a shelf life of only five days.

Pooled Platelets. About four to five platelet units of the same ABO type as the patient are pooled together to make a platelet transfusion for an adult. One unit

may be sufficient for an infant. Cryoprecipitate can be made from the plasma, or the plasma can be stored in a freezer for a year. During this time it may be used for transfusion or processed further.

Pheresis Platelets. In addition to whole blood donations, some components, such as platelets, can be collected by apheresis. With apheresis, a healthy donor comes into the blood center or collection site and the donor's blood is drawn into a machine where the blood is separated into its components. The cell separator collects only the part of the blood that is needed by the patient and the rest of the blood is returned to the donor. This allows a much larger amount of a blood component to be harvested from a single donor. Also, the donor can be specifically selected for (matched with) the patient and the donor can donate more frequently, because he or she does not lose red cells. Pheresis platelets are widely used.

Pheresis platelets have a larger volume of plasma from a single donor, and if the donor and patient platelets are not ABO identical, the patient has a higher risk for acute hemolytic transfusion reaction (see page 16). For the same reason, there may be a higher incidence of transfusion-related acute lung injury (TRALI) (see page 16). To avoid this, many blood centers are now only collecting pheresis platelets from donors who do not have HLA antibodies (antibodies that may form as a result of a challenge to the immune system, pregnancy or organ or tissue transplant).

In most hospitals either pooled platelets or pheresis platelets are available. Most experts consider pooled platelets and pheresis platelets to be interchangeable with regard to increasing the patient's platelet count and controlling bleeding. Both products can be tested for bacterial contamination.

Safety of Blood Transfusions

Autologous and Directed Donations. Autologous donation, in which the patient donates up to 3 units of his or her own blood to be re-infused later, is possible for healthy patients who are undergoing a one-time surgery. However, for patients who are being treated for blood cancers, such donations are not possible because their own blood lacks adequate numbers of cells.

Some family members ask about "directed donations" in which the family chooses its own donors for the patient, believing this may be safer. Although this is possible if a small number of red cells are to be used, e.g., for a surgical procedure, there is no evidence that these donations are any safer than the general blood supply. In fact, under certain circumstances they may be less safe, because related individuals or friends may not wish to expose a circumstance that makes them unsuitable for donation. For patients such as those with blood cancers, the need for long-term blood support, and for specialized components, usually makes this approach unfeasible.

Donor Screening and Collection. Both patients and doctors are concerned about the safety of the blood supply. Today, in medically advanced countries, the benefits of transfusion usually outweigh blood safety concerns for patients with cancer. The risk of transmitting viral diseases such as human immunodeficiency virus (HIV) and hepatitis by blood transfusion has dropped dramatically in the last 25 years. This is the result of a multilayered approach to safety. First, a voluntary blood donor pool eliminates individuals who might donate for money and not be honest about their health history. Public education is important so that people know that certain diseases can be transmitted by blood, what the risk factors are for carrying infectious agents and who should refrain from donating because they are not suitable donors. All potential donors receive written information to urge them to not donate if they are at risk of transmitting a disease through their blood. Once a donor comes to a blood donation site, he or she is screened by trained personnel using a very detailed medical history coupled with a pertinent physical examination. This ensures that the procedure will be safe both for the donor and the blood recipient.

Blood is collected using a new sterile needle and bag after a meticulous cleaning of the donor's arm. Needles are never reused, so there is no risk of infections being transmitted to the donor. Extra tubes of blood are drawn for the laboratory testing. All units are checked for their ABO and Rh blood group to ensure there are no red cell antibodies in the donor's plasma that might injure the patient's red cells.

Testing for Carriers of Infectious Disease. Twelve screening tests for seven infectious diseases are performed on each unit of donated blood. These tests have become more sensitive over the years. Most of these are indirect tests that detect antibodies against the infectious disease. The tests detect antibodies to

- Syphilis
- Human immunodeficiency virus (HIV-1 and HIV-2)
- Hepatitis B virus core antigen
- Hepatitis C virus
- Human T lymphocytotropic viruses (HTLV-1 and HTLV-2).

In addition, tests are performed for hepatitis B virus surface antigen, the protein coat of the hepatitis B virus. Sometimes additional testing is needed for individual patients, such as for cytomegalovirus (CMV) antibodies.

In mid-1999, nucleic acid testing (NAT) for HIV and the hepatitis C virus was added to the testing. This is a highly sophisticated and sensitive means of detecting the genetic material of the virus rather than relying on identifying the development of an antibody in the donor. These tests have further reduced the chance of transmitting the hepatitis C virus or HIV.

The table below shows the current estimates for the residual risk of disease transmission through blood transfusion.

Infectious Disease Risk Estimates for Blood Transfusion in the United States		
Virus	Test(s)	Risk per Unit
Human Immunodeficiency Virus (HIV)	Anti-HIV HIV RNA (MP-NAT)*	1:2 million
Hepatitis C Virus (HCV)	Anti-HCV HCV RNA (MP-NAT)	1:1.6 million
Hepatitis B Virus (HBV)	HBs Antigen Anti-HBc HBV DNA	1:400,000
Human T Cell Lymphotropic Virus (HTLV)	Anti-HTLV	1:109,000
Bacteria in Apheresis Platelets	Bacterial culture	1:109,000
West Nile Virus	WNV RNA (MP-NAT) (ID-NAT)**	1:4.5 million

* MP-NAT- minipool nucleic acid-amplification test
 ** ID-NAT- individual donor nucleic acid-amplification test

Source: American Red Cross, unpublished data from 2010.

The risk of bacterial infection from a unit of red cells that has been routinely stored at 4°C is thought to be about 1:1 million. Because platelets have to be maintained at room temperature to preserve their function, the risk of bacterial growth is higher. Bacterial testing was introduced in 2004 for pheresis platelets and the residual risk of bacterial infection is now calculated as 1:109,000.

Much research is being focused on methods to inactivate viruses in blood components. Some coagulation factors, such as factors VIII and IX, are made from plasma and can be heat-treated to inactivate viruses that might have been present in plasma. Fresh frozen plasma can also now be processed by a technique called “solvent detergent treatment,” which eliminates viruses such as HIV and hepatitis B and C viruses. These viruses have fatty membranes that are destroyed by the detergent.

Coagulation factors are manufactured from pools of 1,500 donated units. These products are treated by inactivation techniques and thus are not infectious for

viruses, such as HIV and hepatitis B and C. It is expected that similar technology may become available for a single unit of plasma, further decreasing the risk of viral contamination.

Blood cells are fragile, and the plasma in which they are suspended cannot be virally inactivated by harsh procedures such as detergent treatments. Research is under way to look at gentler techniques for virally inactivating red cells and platelets.

Removing White Cells. White cells contaminate the red cell and platelet components. These cells are of no use to the patient and are associated with many reactions during and after transfusion. The standard blood filter does not remove such small cells. However, special filters have been developed that can remove up to 99.99 percent of these cells. The technical term for the process of removing white cells (leukocytes) from blood components is “leukoreduction.” This process used to be done at the bedside as the blood was being given to patients. Now that removal of white cells is more common, white cell reduction is often done at blood centers at the time the components are prepared. This ensures that the filtering is consistent and components can be tested to ensure that white cell reduction has been achieved. In many industrialized countries removal of white cells from red cell or platelet components is now standard practice. In the United States, leukoreduction is frequently used but it is not a universal practice. Patients requiring transfusion should ask their doctor about the use of leukoreduced blood components.

Transfusions for Patients with Blood Cancer

This section contains information that applies to leukemia, lymphoma, myeloma, myelodysplastic syndromes, myeloproliferative neoplasms and other hematological conditions, such as hereditary anemias and aplastic anemia. In particular, blood or marrow stem cell transplantation for patients with these diverse diseases invariably involves frequent blood transfusions. This occurs because the basis of the transplant treatment is to give very high doses of chemotherapy to the patient to maximize the chance of a cure. Many drugs used for chemotherapy cause temporarily impaired blood cell production in the marrow and depressed immune system functions.

The disease processes of leukemia, myeloma, and many lymphomas interfere with the normal production of red cells, white cells and platelets in the marrow. Thus, it is common for patients with these diseases to develop anemia (a low red cell count), thrombocytopenia (a low platelet count) and in some cases, leukopenia (a low white cell count). This can happen before treatment begins, since the cancer cells inhibit the production of normal blood cells in the marrow. In addition, the drugs used to treat these diseases—which stop disease progression or, in some cases, cure these diseases—often injure healthy stem cells in the marrow as a

side effect. These injured cells would normally go on to produce red cells, white cells or platelets. Temporary side effects such as very low red cell or platelet counts can occur for a few weeks, in most cases, because fewer healthy cells are being made.

The need for transfusions varies, depending on the type of blood disease in question and the type of drugs used in the treatment. For example, almost all patients with leukemia (a disease primarily affecting the marrow and blood) require some transfusions during their care. Many patients with Hodgkin or non-Hodgkin lymphoma (diseases primarily affecting the lymph nodes and spleen) may not require transfusions unless they require a blood or marrow stem cell transplant or if the lymphoma involves the marrow.

Individual doctors take different approaches in deciding if transfusion is appropriate for a given patient, because there is controversy as to how to best balance the benefits and risks of transfusion in many clinical situations. Studies comparing various indications for transfusions may help doctors have a more scientific basis for their decisions, but currently, transfusion policies usually depend on the patient's condition and an individual doctor's training, experience and long-held community standards of practice. The trend in the last few years is to be considerably more conservative in the use of transfusion products where possible.

Red Cells and Platelets. During and after chemotherapy, it is possible to replace the red cells and platelets with cells donated by healthy volunteers via blood transfusions. Severe anemia (a relative term, not well-defined by scientific studies) or thrombocytopenia can be life-threatening in extreme cases. Most doctors specializing in the care of patients with blood cancers believe that varying degrees of replacement by prophylactic red cell transfusion represents a good practice to prevent complications of anemia, such as fatigue, weakness, shortness of breath or in extreme cases, heart attack or stroke. Similarly, most doctors advocate giving prophylactic platelet transfusions to reduce the likelihood of bleeding.

White Cells. Unfortunately, practical methods of safely and effectively transfusing adequate numbers of granulocytes or other white cells are not yet available to prevent infection that occurs as a result of a low white cell count. White cell transfusion is usually reserved for uncommon instances of severe infections with bacteria or fungi that do not respond to antibiotics or antifungal drugs.

Because the yield of white cells from current collection techniques is insufficient, some investigative studies and clinical protocols now involve administering white cell growth factors (e.g., granulocyte-colony stimulating factor [G-CSF]) to volunteer donors, particularly family members, prior to white cell collection by apheresis. This increases the number of white cells that are in the donor's circulation, thus improving the yield of white cells collected. It is hoped that the larger number of white cells collected in this manner will be more effective in fighting infection.

Transfusion of Red Cells. Red cell transfusions are used to treat low red cell counts (anemia), which, if untreated, can cause weakness, lethargy and in extreme cases, more severe symptoms such as shortness of breath or rapid heartbeat. Most doctors prescribe red cell transfusions before a patient develops serious symptoms, particularly when managing older patients or those with a history of heart or blood vessel disease.

There are few scientific data that guide doctors as to the exact red cell count at which to prescribe a transfusion. The age of the patient, the level of his or her activity, the presence of other complicating medical conditions and the likelihood and timeliness of the recovery of red cell production in the marrow each must be considered along with the red cell count.

All red cell transfusions need to be matched to the patient in the laboratory, and for patients with blood diseases the donated blood should always have the white cells removed by filtration. “Leukoreduced” or “leukodepleted” are the medical terms for white cell removal. Leukoreduction reduces the risks of fever and chills after transfusion, reduces the risk of not responding to platelet transfusions due to the development of human leukocyte antigen (HLA) antibodies and reduces the risk of transmission of some viral infections (e.g., cytomegalovirus, HTLV-1). Some centers use irradiation of all cell transfusions to patients receiving intensive chemotherapy or who are considered to have impaired immune systems to prevent a rare but potentially life-threatening complication of transfusion called “graft-versus-host disease” (GVHD). Patients undergoing blood or marrow stem cell transplants generally should receive irradiated blood components during the transplant period.

Your doctor’s decision to give you red cell transfusions is based on a combination of factors, including

- The level of hemoglobin (the protein in red blood cells that carries oxygen) in your blood
- Whether you have symptoms such as fatigue or shortness of breath
- Any other health complications you may have, such as heart disease.

Iron Overload. The body contains about 2,000 to 3,500 milligrams of iron, most of which is present in red cells. The body has no ability to excrete the excessive amounts of iron resulting from red cell transfusions.

Each red cell unit contains about 250 milligrams of iron, and patients, who have regular transfusions, ranging from less than 2 units to 4 or more units of blood a month, can accumulate too much iron in their bodies as a result. The iron is deposited in tissues and major organs such as the liver, heart and pancreas and can result in serious damage. A patient with iron overload should talk to the doctor about his or her intake of vitamin C and alcohol, both of which increases absorption of iron.

If you're receiving transfusions, your doctor may monitor you for iron overload with a blood test called a "serum ferritin level," which measures your body's iron store. You may need a drug called an "iron chelator" to remove excess iron from your body because of transfusion-dependent anemias. Be sure to talk with your doctor about the potential benefits and risks of using these drugs.

Iron overload is generally not a risk for a patient who has received less than about 20 red cell transfusions over his or her lifetime.

Transfusion of Platelets. Platelet transfusions are given to prevent or to treat bleeding due to severely low platelet counts (thrombocytopenia). There is controversy as to whether prophylactic platelet transfusions are necessary or beneficial, although it seems that maintaining a platelet count of greater than 5,000 microliters (μL), and sometimes higher, reduces the risk of minor bleeding (e.g., nose bleeds, bruises in the skin called "ecchymoses," pinpoint bleeding in the skin called "petechiae"). The platelet count at which most hematologists and oncologists believe prophylactic transfusion (in the absence of bleeding) is indicated has decreased from about 20,000 μL to 10,000 μL at most cancer centers, but there is great individual variation from doctor to doctor within this range, and from patient to patient. It is uncommon for patients to bleed when their platelet counts go below 30,000 μL , and most patients can tolerate stable platelet counts within a range of 5,000 μL to 10,000 μL without bleeding. The need for surgery or other invasive procedures often requires transfusion to maintain a much higher platelet count during surgery and for a period of healing thereafter.

Platelets can be given as pools made from several units of whole blood from different donors, or single donor units obtained by apheresis (see page 8). Donated platelet units should have the white cells removed by filtration prior to transfusion and, if appropriate, should be irradiated as well.

Transfusion of Granulocytes. A patient who has few or no circulating white cells may develop an infection that does not respond to antibiotics. In some such instances, use of apheresis to collect donor granulocytes may permit their transfusion and provide some benefit until the patient's own white cell counts recover. As with red cells and platelets, these transfusions should be irradiated prior to transfusion, but should not be treated with leukoreduction filters, as this would defeat the purpose of transfusing white cells. The white cells are infused through a standard blood filter that does not filter out white cells, but will filter out any particles or clotted blood elements. There is uncertainty over whether current methods of granulocyte collection produce an effective transfusion, which is why some protocols now include G-CSF stimulation of the granulocyte donor.

Transfusion of Plasma and Cryoprecipitate. Fresh frozen plasma (FFP) and cryoprecipitate, often called "cryo" for short, are transfused to patients who

have abnormal or low levels of blood-clotting proteins, as in hemophilia. Clotting protein abnormalities in the plasma may develop in patients with poor clotting factor production due to liver disease or increased use of clotting factor proteins due to infection. Fortunately, these conditions are uncommon in patients with hematologic malignancies, with the exception of promyelocytic leukemia. In this type of leukemia, abnormal clotting can occur and it may be necessary to transfuse these liquid fractions of donor blood to prevent or to treat bleeding.

Use of Intravenous Gamma Globulin (IVIG). Gamma globulin prepared from a pool of donor plasma is sometimes given to patients with hematologic diseases to supplement their low levels. Very low gamma globulin levels are a frequent feature of chronic lymphocytic leukemia. Severely low levels of gamma globulin can lead to an increased risk of some types of bacterial infections. Gamma globulin may also be of use in reducing the risk of cytomegalovirus disease and other immune complications of the hematologic disease or its treatment. Gamma globulin is specially treated by techniques that cannot be used for cell transfusions; it does not carry the risk of transmission of viruses such as hepatitis C virus or human immunodeficiency virus (HIV). Most side effects are very modest and can include mild headache, rash or hives.

Transfusion of Albumin. Rarely, transfusion of the most common human blood protein, albumin, is needed in patients who have severe liver malfunction. Albumin does not carry a risk of transmission of viruses such as hepatitis C virus or HIV. Side effects are uncommon with albumin transfusions.

Palliative Care and Transfusions. Palliative care is a form of medical care that focuses on improving the quality of life for patients facing serious illness. The goal is to prevent and relieve pain and other symptoms and to provide psychological, spiritual and emotional support. Palliative care is appropriate from the time of diagnosis and is provided along with curative treatment. Blood transfusions can be used as palliative care. Healthcare coverage for palliative care may differ based on what treatments are needed. There are doctors and nurses who specialize in palliative care and who may be part of the patient's medical care team, or the patient's hematologist/oncologist may manage this aspect of care.

Hospice care (care for patients who are thought to have less than six months to live) can continue to provide palliative care for patients. The aim of hospice care is to provide the best possible quality of life and to relieve pain and symptoms during the final days of a person's life at a time when the underlying disease can no longer be treated or cured. Blood transfusions are less frequently used during this time and are only used when the goal is to alleviate pain and discomfort and enhance the quality of life, not cure the disease.

Complications of Blood Transfusions

Most transfusions are not associated with adverse reactions. However, reactions can occur with any blood component. The reaction may occur at the time of the transfusion, such as abrupt high fever (called a “febrile reaction”) or the destruction of the transfused red cells (called a “hemolytic reaction”). Transfusion-related acute lung injury (TRALI) is the term for new-onset of acute lung injury (ALI) that occurs within six hours after the transfusion of a plasma-containing blood product. The cause of TRALI is currently not fully understood. TRALI is treatable with supportive care, but can be fatal if recognition of TRALI is delayed. Other deleterious effects, such as the transmission of viruses, are not apparent until weeks or months later, after the incubation period and the onset of the viral disease.

The symptoms of most of the reactions that occur either during or soon after transfusion are similar. These include the development of a fever, chills, nausea, pain at the site of the transfusion (an arm vein) or in the back, shortness of breath, a drop in blood pressure, passing dark or red urine or a rash. Any patient noticing any change in his or her condition during a transfusion, however slight it may seem, should alert the nursing staff promptly. Serious complications can be prevented by early recognition of a reaction, stopping the transfusion and limiting the amount of blood given.

The initial management of all transfusion reactions is the same (except for when the only reaction is hives. See *Reactions that Cause Hives*, on page 17), because the symptoms of different types of reactions may overlap. The transfusion is stopped and the unit is returned to the blood bank for examination to check for factors that might have caused the transfusion reaction. At the same time the intravenous line is retained by infusing a glucose solution in case intravenous fluids or drugs are needed for treatment, and a doctor is called. Blood samples may need to be drawn and treatment started right away. Many transfusion reactions, but not all, can be prevented or minimized by removing white cells from the component either at the bedside or in the blood center at the time of collection. Patients with hematologic diseases usually receive blood component units that are leukoreduced.

Reactions That Damage or Destroy Red Cells. Damage or destruction of the transfused red cells is rare. However, if this does occur, it represents the most severe and important acute reaction associated with blood components. Such a reaction, called an “acute hemolytic transfusion reaction,” can lead to a drop in blood pressure, bleeding or kidney damage, which may be life threatening. Because of this, all reactions are considered serious until a hemolytic reaction has been ruled out. Treatment of a hemolytic reaction includes taking measures to maintain the blood pressure and prevent kidney damage and bleeding.

Reactions That Cause Fever. Reactions that cause fever, referred to as “febrile reactions,” are the most common. These account for more than 90 percent of

all transfusion complications. Fever is sometimes accompanied by chills, and on some occasions, shortness of breath. These reactions are frightening and uncomfortable for the patient but are usually not serious. However, they must be distinguished from the more serious acute hemolytic transfusion reaction mentioned on page 16. While the reaction is being investigated, the transfusion is delayed. Treatment may be given to reduce the elevated temperature. Medicines can be given before the transfusion to prevent such a reaction. A fever reaction is most commonly caused by antibodies to the small number of white cells mixed with the red cells. The use of red cells from which white cells are removed before storage of the unit is the most effective means of preventing the high fever and chills.

Unfortunately, during platelet transfusions, reactions causing high fever and chills are more frequent, because the cause of these reactions is more complex. Filtering out white cells at the bedside is not as useful in preventing these effects as it is with red cells. Prestorage leukoreduction is required. Washing of platelets before transfusion removes certain substances that form immune complexes. In addition to leukoreduction, washed platelets are occasionally requested for patients with histories of allergic or anaphylactic reactions.

Reactions That Cause Hives. Hives, which usually itch, are the second most common side effect of transfusion. The medical term for hives is “urticaria.” The skin changes are presumably due to soluble substances in the plasma of the donor that cause an allergic reaction in the patient. These reactions are not dangerous, but they do cause discomfort and anxiety to the patient. They can be treated with an antihistamine. For subsequent transfusions to susceptible individuals, the antihistamines can be given beforehand to prevent a reaction. This is the only reaction that does not necessarily require discarding the unit. If hives are present without any other symptoms, the transfusion can be restarted slowly once the hives have resolved.

The Patient Makes Antibodies to the Donor’s Blood. Some patients may produce antibodies against certain antigens in transfused blood. Although blood is typed for the most important antigens on the red cell, ABO and Rh, there are many other antigens on red cells, white cells, platelets or occasionally in the plasma that can cause a patient to make antibodies against the donor blood. The medical term for this phenomenon is “alloimmunization.” This effect does not necessarily cause immediate symptoms but is important if subsequent transfusions are needed. With red cell transfusions the situation can be managed by selecting donors for future transfusions with red cells that do not carry the antigens to which the patient has made an antibody. The compatible blood can usually be obtained by testing the units in the blood bank. However, occasionally a blood unit may need to be shipped in from another blood center or a rare donor registry. This type of exchange between blood centers is a common practice and provides a national pool of blood.

With platelet transfusions, the antibodies are formed against white cells. However, these antibodies may also destroy the transfused platelets. Specifically matched platelets will need to be collected if this occurs. Most blood centers have a pool of volunteer blood donors who have been human leukocyte antigen (HLA) typed and are willing to donate by apheresis. The platelets will then all come from a few specifically matched donors who each provide a large dose of platelets. A donor's propensity to make antibodies to white cells can be reduced—but not completely prevented—by the transfusion of red cells and platelets only, with the white cells removed.

Transmission of Viral Infections. Blood is a biological substance and transfusion may never be risk-free. While the chance of getting a viral disease following blood transfusion has decreased markedly in the last 20 years, the risk has not been eliminated. Indirect tests, using detection of antibodies to the viruses, cannot detect infections that occur between the time of exposure to the virus and the appearance of the antibody. This period is referred to as the “window period,” and if a donation is made during this time there remains a very small residual risk of viral transmission. This is one reason why a careful interview to screen out donors who are at risk for a transmissible virus infection remains an important aspect of blood safety procedures. Since 1999, the risk of being infected by HIV and the hepatitis C virus has been considerably reduced because of the introduction of the more sensitive nucleic acid testing for these viruses. Now, units that test positive for these viruses are discarded so infection risk is dramatically lower.

Transmission of Cytomegalovirus (CMV). Cytomegalovirus (CMV) is a common virus, and about 50 percent of individuals in the United States have been infected with it by the time they are 50 years old, most without developing symptoms. However, in premature babies and in patients undergoing blood or marrow stem cell transplantation, CMV infection can cause serious problems, such as pneumonia. CMV infection may be due to reactivation of the virus from a previous exposure or from prior blood transfusion. Patients with leukemia and those undergoing blood or marrow stem cell transplantation who have no antibodies to CMV should receive blood components that are negative for CMV antibodies. Since the virus resides in white cells, it can be transmitted by blood components that contain white cells. Removal of white cells from blood components is another approach to preventing CMV. This approach appears to be as efficient as providing components from CMV antibody-negative donors.

Transmission of Bacterial Infections. Infection with bacteria due to a blood transfusion is an extremely rare complication with red cell transfusions, on the order of one per million transfusions. Blood is collected and processed in a sterile system. However, bacteria are very occasionally present in the donor's blood at the time of donation or the blood is contaminated at the time of collection. Red cells that are stored at refrigerator temperatures do not usually provide the right conditions for organisms to grow, so that infection from red cell transfusions is the

least common complication. However, platelets that are kept at room temperature can allow bacteria to grow in a contaminated unit. Therefore, infection following platelet transfusions is more common than it is with red cell transfusions. Culturing all pheresis platelets for bacteria was started in March 2004 in the United States, and methods of doing the same for platelets made from whole blood have been more recently introduced.

Graft-Versus-Host Disease (GVHD). Donor white cells (lymphocytes) can attack the recipient's skin, liver, bowel and marrow after blood or marrow stem cell transplantation. The result of this attack is called "graft-versus-host disease" (GVHD). Donor lymphocytes from a blood transfusion have the potential to produce a similar reaction in the recipient. Although this is very uncommon, it may happen in patients who have decreased immune system function, referred to as "immunosuppressed" or "immunocompromised." Immunosuppression can result from a disease or intense or prolonged chemotherapy or radiation therapy. Most centers treat all blood components for transfusion to patients who are severely immunosuppressed with irradiation. Fortunately, this very severe complication is rare and almost never occurs after transfusion of irradiated blood. Recipients of stem cell transplants may develop GVHD, but this complication is usually easier to manage than GVHD resulting from transfusions.

Effect on a Patient's Immune System. There is a controversial theory that transfusions can cause decreases in immune function. The medical term for this effect is "immunomodulation." It is not clear what the implications of this effect, if any, are for patients with blood cancer. In other clinical settings (surgery), filtering out white cells from transfusion components appears to prevent deleterious immune effects of transfusion to a large degree and this process should be used for all patients with blood cancer who receive transfusions.

Resources and Information

LLS offers free information and services to patients and families affected by blood cancers. This section of the booklet lists various resources available to you. Use this information to learn more, to ask questions and to make the most of the knowledge and skills of the members of your healthcare team.

For Help and Information

Consult With an Information Specialist. Information Specialists are master's level oncology social workers, nurses and health educators. They offer up-to-date disease, treatment and support information. Language services (interpreting and translation) are available. Please contact our Information Specialists or visit our website for more information.

- Call: (800) 955-4572 (Monday through Friday, from 9 am to 9 pm ET)
- Email: InfoCenter@LLS.org
- Live online chat: www.LLS.org/InformationSpecialists
- Visit: www.LLS.org/InformationSpecialists

Clinical Trial Support Center. Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.

Free Information Booklets. LLS offers free education and support booklets that can be either read online or ordered. Please visit www.LLS.org/booklets for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

Financial Assistance. LLS offers financial assistance to individuals with blood cancer. Please visit www.LLS.org/finances for more information.

Co-Pay Assistance Program. LLS offers insurance premium and medication co-pay assistance for eligible patients. Please call or visit our website for more information.

- Call: (877) 557-2672
- Visit: www.LLS.org/copay

LLS Health Manager™ App. This free mobile app helps you manage your health by tracking side effects, medication, food and hydration, questions for your doctor, and more. Export the information you've tracked in a calendar format and share it with your doctor. You can also set up reminders to take medications, hydrate, and eat. Visit www.LLS.org/HealthManager to download for free.

One-on-One Nutrition Consultations. Access free one-on-one nutrition consultations provided by a registered dietitian with experience in oncology nutrition. Dietitians assist callers with information about healthy eating strategies, side effect management and survivorship nutrition. They also provide additional nutrition resources. Please visit www.LLS.org/nutrition to schedule a consultation or for more information.

Podcast. *The Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other healthcare professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Visit www.LLS.org/TheBloodline for more information and to subscribe.

Suggested Reading. LLS provides a list of selected books recommended for patients, caregivers, children and teens. Visit www.LLS.org/SuggestedReading to find out more.

Continuing Education. LLS offers free continuing education programs for healthcare professionals. Please visit www.LLS.org/ProfessionalEd for more information.

Community Resources and Networking

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Please visit www.LLS.org/community to join.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients reach out and share information. Please visit www.LLS.org/chat to join.

LLS Chapters. LLS offers community support and services in the United States and Canada, including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), in-person support groups and other great resources. For more information about these programs or to contact the nearest chapter, please call or visit our website.

- Call: (800) 955-4572
- Visit: www.LLS.org/ChapterFind

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, please visit www.LLS.org/ResourceDirectory to obtain our directory.

Advocacy. The LLS Office of Public Policy (OPP) engages volunteers in advocating for policies and laws that encourage the development of new treatments and improve access to quality medical care. Please call or visit our website for more information.

- Call: (800) 955-4572
- Visit: www.LLS.org/advocacy

Additional Help for Specific Populations

Información en español (LLS Information in Spanish). Please visit www.LLS.org/espanol for more information.

Language Services. Let members of your healthcare team know if you need translation or interpreting services because English is not your native language, or if you need other assistance, such as a sign language interpreter. Often these services are free.

World Trade Center (WTC) Survivors. People involved in the aftermath of the 9/11 attacks who were subsequently diagnosed with a blood cancer may be eligible for help from the World Trade Center (WTC) Health Program. People eligible for help include:

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were either in the NYC disaster area, or who lived, worked or were in school in the area
- Responders to the Pentagon and the Shanksville, PA crashes

For more information, please call the WTC Health Program or visit their webpage.

- Call: (888) 982-4748
- Visit: www.cdc.gov/wtc/faq.html

People Suffering from Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time, for example, if you feel depressed every day for a 2-week period. For more information, please call the National Institute of Mental Health (NIMH) or visit their website.

- Call: (866) 615-6464
- Visit: www.nimh.nih.gov and enter “depression” in the search box

References

American Red Cross. www.redcrossblood.org

Fang CT, Chambers LA, Kennedy J, Strupp A, Fucci MC, Janas JA, Tang Y, Hapip CA, Lawrence TB, Dodd RY; American Red Cross Regional Blood Centers. Detection of bacterial contamination in apheresis platelet products: American Red Cross experience, 2004. *Transfusion*. 2005;45(12):1845-1852.

Spinelli SL, O'Brien JJ, Bancos S, Lehmann GM, Springer DL, Blumberg N, Francis CW, Taubman MB, Phipps RP. The PPAR-platelet connection: modulators of inflammation and potential cardiovascular effects. *PPAR Research*. 2008; 2008: 328172. Published online 2007 December 24. doi: 10.1155/2008/328172.

The 2011 National Blood Collection and Utilization Survey Report. American Association of Blood Banks and the US Department of Health and Human Services, 2011. <https://www.hhs.gov/oidp/initiatives/blood-tissue-safety/initiatives/national-blood-collection-and-utilization-survey/index.html>



Get support. Reach out to our **INFORMATION SPECIALISTS**

The Leukemia & Lymphoma Society team consists of master's level oncology social workers, nurses and health educators who are available by phone Monday through Friday, 9 a.m. to 9 p.m. (ET).

- Get one-on-one personalized support and information about blood cancers
- Know the questions to ask your doctor
- Discuss financial resources
- Receive individual clinical-trial searches

Contact us at

800-955-4572 or
**www.LLS.org/
informationspecialists**

(Language interpreters can be requested)





For more information, please contact our Information Specialists **800.955.4572** (Language interpreters available upon request).

**BEATING
CANCER
IS IN
OUR BLOOD.**

National Office 3 International Drive, Suite 200 Rye Brook, NY 10573

The mission of The Leukemia & Lymphoma Society (LLS) is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families. Find out more at www.LLS.org.