Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

B. Blood Donation

Chapter 11

Blood Donation and Collection

Gary Zeger • Eileen Selogie • Ira A. Shulman

Blood donation is critical to all of transfusion therapy, as it provides the starting product. In the United States and many other economically developed nations, all of the blood is given by volunteer, nonremunerated donors. Donated whole blood is then made into transfusable components, which include but are not limited to packed red blood cells (RBCs), platelets, and frozen plasma or cryoprecipitate. Other lesser utilized blood components, such as granulocytes and cryoprecipitate-depleted plasma, also have important therapeutic value. Individual plasma proteins, such as factor VIII, have been manufactured using recombinant methods for years; however, there is no commercial product, single or combined, with the clinical properties of frozen plasma. Each of these components make possible an extraordinary number of traditional and state-of-the-art medical therapies, including trauma surgery, organ transplantation, and cancer chemotherapy. At the time of this writing, there are no clinically effective or available substitutes for RBCs, platelets, or plasma in the United States.

In 2001, the National Blood Donor Resource Center estimated that 8 million volunteer U.S. blood donors contributed approximately 15 million whole blood donations per year, the majority of which were manufactured into separate components, such as RBCs, fresh frozen plasma, and platelets.[1] These components allowed transfusion of 29 million blood components in the United States. Thus, in the United States, the average volunteer blood donor gives blood about 1.6 times a year. Of that total, almost 2% represent donations indicated for a specific recipient other than the donor. These are generally referred to as *directed* or *designated donations.* In addition, approximately 3% of blood donations are *autologous:* blood that is donated by an individual for his or her own use, usually for a prescheduled elective surgery.[2–4] Although it is estimated that 60% of the adult population in the United States is eligible to donate blood, at present it is believed that less than 5% of the eligible population donates within any given year.[5,6] The various reasons that some people give blood readily and others do not have been studied for several decades, but the blood donation process and applicable statistics during this time have changed little, if at all.

THE PROCESS OF BLOOD DONATION

Blood donation can be divided into five processes that are directly related to the donor: recruitment, screening, physical examination, collection, and post-donation care.

Recruitment of blood donors is a specialized task. It is often performed by telerecruiters, and the message delivered must be convincing and compelling to result in a scheduled appointment to donate blood.

Once a donor has been recruited, the screening process is carried out to make sure that the donation process will be safe for the donor and that the collected blood will be safe for the recipient. The prospective donor is initially given information about criteria for eligibility for blood donation and about the process itself. The screening process consists of a questionnaire that seeks to find medical conditions and behaviors that might make donation unsafe for the donor or recipient. Critical information is confirmed by direct verbal questioning to ensure that the answers are accurate. If no disqualifying information is uncovered during the screening process, a brief physical examination follows, which includes examination of antecubital veins, followed by measurement of body temperature, donor hematocrit or hemoglobin, and heart rate.

After the venipuncture is performed, blood is collected, labeled, and temporarily stored until it can be transferred to a manufacturing center for further processing and distribution. Specimen tubes are drawn at the time of collection for infectious disease testing; these tubes are sent for testing immediately after collection.

After the donation, donors receive oral fluids and remain under observation for a period of time so that any post-donation reactions may be treated appropriately. Post-donation instructions are given to help the donor avoid untoward side effects. The donor is instructed to call the blood center with any post-donation information, such as the development of worrisome physical symptoms or information remembered that would change the answers given during the screening process.

Donor Recruitment

Maintaining an adequate blood supply is an ongoing challenge. Attrition of blood donors due to older age and illness, implementation of new regulations resulting in deferrals, or other reasons makes it difficult for blood collection centers to keep pace with the increasing demand for blood. Thus, the recruitment of new blood donors must be ongoing and vigorous. New exclusionary criteria and serologic testing make this task increasingly difficult, as does the fact that newly recruited blood donors are nearly twice as likely to have disqualifying medical conditions as are established blood donors.[7]

It is unacceptable to provide volunteer blood donors with monetary compensation (i.e., cash or cash equivalents), so the act of blood donation in the United States is voluntary. Thus, without paying donors for their time and blood, the

formidable challenges of encouraging volunteer blood donation begin at the first step of the blood collection process: donor recruitment.

Sources of Donor Motivation

The most successful approach to recruitment of volunteer blood donors has been an appeal to community responsibility. Individuals often first learn about the need for donation during blood shortages via public service announcements and appeals for blood from newspapers, radio, and television. Other donors become aware of the importance of blood donation when transfusions are needed for family and friends (or themselves).

Appeals after disasters tend to bring out community spirit in Americans. This was particularly evident after the September 11, 2001, terrorist attack on the New York World Trade Center and the Pentagon in Washington, D.C. In both instances, blood donations vastly exceeded the local demand, due to the motivation of the entire community to contribute to their fellow Americans in need.

Donating blood for a friend or relative (directed donation) has proven to be an excellent motivator and has brought many first-time blood donors into the system. Donating for one's own use (autologous donation) has also been an effective motivator.

For whatever reason each donor is motivated to give blood, he or she must be convinced that donation is truly necessary and will be appreciated. For this reason, appeals for blood should only be made when there is a significant shortage. Once the donor has been motivated to donate, making his or her blood donation a convenient and pleasant experience is critical to retaining that donor for subsequent donations. Excellent customer service is the key to retaining blood donors.

A Note about Minority Donors

Latino Americans, particularly immigrants from Mexico, are the largest growing demographic group in the United States.[8] Adequate donor recruitment and collection among this minority group is especially important because of the high percentage of blood group O among Latinos. Because group O individuals can only receive group O RBCs, a higher percentage of group O blood is necessary in areas with large Latino populations. Specialized recruiting programs are important to attract and maintain these essential donors. Appeals in Spanish to Latino organizations and in the media are of key importance. In areas with large Latino populations, an effort should be made to provide Spanish versions of all donor materials. It is also advisable to have staff members who are conversant in Spanish or to have translators readily available.

With the exception of Chagas disease, the incidence of infectious disease markers among whole blood donors in areas with large Latino populations is similar to that of other repeat whole blood donors.[9] However, the seroprevalence of Chagas disease among whole blood donors in Los Angeles is 1 in 7200, versus 1 in 93,000 among plateletpheresis donors.[10] The significant difference in this seroprevalence is due to the fact that very few Latino individuals donate apheresis platelets in Los Angeles.

African American donors are currently the second largest minority population in the United States.[9] Recruitment and donation by African Americans is particularly important, due to many factors: they make up a large percentage of the general eligible blood donor population in certain communities; the high prevalence of blood group B in the African American population; and the higher prevalence of African Americans with specific blood types (e.g., antigen-negativity for a variety of RBC antigens to which antibodies are frequently made in highly transfused populations, such as patients with sickle cell disease) that may be used for patients who have made antibodies to these antigens.

Few publications adequately address the reasons why certain minority populations do not donate blood at the same percentages as the white population. Much research is necessary to understand the needs and wants of these important donors, so that these minority donors can be successfully recruited into the blood donor system.

Paid Donors

Aside from paid plasma donors at centers that manufacture fractionated, licensed plasma products, it is not acceptable to provide monetary compensation (cash or cash equivalents) to blood donors in the United States. In the early days of blood banking, paying for blood donors was a commonplace and accepted practice. These donors were often motivated by a lack of funds to maintain drug or alcohol habits; subsequently, paid donors had a higher incidence of transfusion-transmissible diseases, particularly hepatitis, which infected many early blood recipients. In the 1970s, growing recognition of this problem[11] led the Food and Drug Administration (FDA), in its Code of Federal Regulations (CFR), to require blood from paid donors to be labeled as such.[12] As these "paid donor"-labeled units were considered to be undesirable by clinicians and hospitals, the practice of paid whole blood donations effectively died out.

In some states, however, the shortage of single donor platelet concentrates collected by apheresis technology prompted exceptions for these donations. Until January 1, 2003,[13] a few U.S. blood collection facilities continued to pay apheresis donors. Due to the previous stigma attached to paid blood donation, these centers employed screening procedures that met or exceeded those of "all-volunteer" centers. Despite studies demonstrating that these donors had infectious disease marker frequencies similar to, or better than, those of volunteer donors, these centers were eventually forced to cease paying plateletpheresis donors.[14]

Paid donation, however, is regularly utilized for the recruitment of donors in the United States for commercial source plasma. This plasma is collected by apheresis and sent for further manufacture into various plasma-derived products. Because the pooled plasma from these donations is effectively "sterilized" during the fractionation and manufacturing process, there is less concern about the potentially increased risk for infectious disease transmission by using paid donors for "source plasma." Most countries with all-volunteer commercial plasma programs have struggled, usually unsuccessfully, to meet their population's plasma derivative needs.[15]

Health Benefits of Whole Blood Donation

The proven health benefit to blood donors is the free mini-physical examination and the infectious disease screening testing performed at the time of donation. Many donors might not have otherwise become aware of diseases such as hypertension, anemia, cardiac arrhythmia, hepatitis, or human immunodeficiency virus (HIV)

infection. This information alerts the donor to seek further appropriate medical diagnosis and treatment, and may limit the transmission of infectious disease to others. Aside from these benefits, a controversial hypothesis that depletion of iron stores through whole blood donation can improve cardiovascular status[16,17] has been proposed; more research needs to be performed prior to making any claims regarding cardiac health benefits from blood donations.

Donor Incentives

Improved screening and infectious disease testing methods used for donor blood have made widespread infectious disease transmission by transfusion, as occurred in the early days of paid blood donors, a thing of the past. All-volunteer donor programs have become the base of the blood collection establishment. Although blood donor incentives such as t-shirts, gift certificates, and paid time off are acceptable gifts, rewards that can easily be converted to cash (or cash itself) are not. The issue of donor motivation caused by incentives continues to be an area of concern to the FDA and the American Association of Blood Banks (AABB). The CFR, in its definition of paid and volunteer donors, states that "Benefits, such as time off from work, membership in blood assurance programs, and cancellation of nonreplacement fees that are not readily convertible to cash, do not constitute payment within the meaning of this paragraph." The AABB[18] and FDA[19] have provided some guidance on donor incentives (Table 11–1). There is still a concern that a potential donor might be untruthful about high-risk behaviors for infectious disease to receive a gift being offered at a blood collection site. For this reason, incentives should be provided for simply attending a blood drive and attempting to donate, rather than the gift being given based on the condition of the actual donation.

Blood Credit Programs

Blood credit programs, which in the past were more popular entities, are difficult to manage logistically and practically. The implication that a blood donor will receive a credit that can eventually be cashed in for "free" blood in the future is almost always misleading. The credits are often symbolic "credits to the blood supply" and have no direct application to the donor, monetarily or otherwise. The logistics of a true crediting program are generally prohibitive, because the time and place that the credits will be redeemed is unknown, and the involved health care providers may not be party to the program.

Patients are sometimes encouraged to have friends and relatives donate blood to "replace" any that they might use. This appears to be a reasonable recruitment strategy, as long as the patient is not made to feel stressed and anxious about finding replacement donors. It is most important for the patient to understand that he or she will never be denied blood because of inability to replace blood that has been, or might be, used. Poor communication, however, might cause the patient to put blood donation pressure on family, friends, and acquaintances who may have valid reasons for not donating, thus potentially endangering the blood supply.

Motivation by Free Testing

A serious concern throughout the blood industry following the discovery of HIV in the early 1980s (and the subsequent knowledge that HIV was transmissible through transfusions), was that high-risk individuals would donate blood to obtain a free confidential HIV test. The concern that people might now donate blood to receive free blood tests (a magnet effect) has been shown to be generally unfounded, at least for HIV p24 antigen testing.[20] Nevertheless, donor centers generally make available a list of testing sites where confidential or anonymous HIV blood testing is available, to discourage a potential high-risk individual from donating.

Factors for Success

Any donor's internal motivation will only provide a finite amount of impetus for continued participation in the blood donation process. It is the job of the entire blood collection team to make the donation process as pleasant as possible. If they are successful, a hesitant first-time donor may be converted into a regular repeat blood donor. This is a worthwhile goal: regular, repeat blood donors are more reliable and have less risk of infectious disease.

Making blood donation as convenient as possible is of prime importance. After a national disaster, blood donors have stood in long lines for hours to donate blood for anonymous victims. In such times, the truly heroic nature of the motivated blood donor is evident. Under more routine circumstances, inhospitable conditions and/or poor customer service may almost certainly discourage a blood donor from making a donation. A safe and convenient location is critical to attract and retain repeat blood donors. Parking should be easily available and free. The waiting area should be clean and pleasant. Excessive waits are to be avoided, and donors should be given an accurate wait-time whenever possible. Blood center staff should be professional, knowledgeable, and courteous. Of particular importance is making sure

Table 11–1 **Examples of Donor Incentives.**

Items Considered "Paid" Incentives	Items That May Qualify as "Nonpayment"
Cash payment or cash equivalent	Tokens or prizes of nominal value (e.g., coffee cups, t-shirts, pins)
Tickets to concerts or sporting events where market for resale exists	Employee paid time off
Music media not associated with product promotions where market for resale exists	Raffle tickets, regardless of value of prize. Prize must not be transferable or readily convertible to cash
Transferable product discounts or coupons convertible to cash	Membership in blood assurance program
Vouchers for free medical tests	Medical tests performed at the time of donation
Scholarships paid directly to students	Scholarships transferred directly to academic institution
	Gift cards and gift certificates that are nontransferable, not redeemable for cash, and bear the donor's name

From Compliance Policy Guide for FDA Staff and Industry, Chapter 2, Section 230.150. Issued May 7, 2002, revised November 22, 2005. Available at http://www.fda.gov/ora/compliance_ref/cpg/cpgbio/cpg230=150final.htm. Last modified December 12, 2005. Accessed June 3, 2006.

that a new donor understands the donation process and fully knows what to expect. Donors appreciate honesty, and unpleasant or painful surprises often provoke bad feelings.

Blood Collection Sites: Fixed and Mobile

Fixed site is a widely used term for a permanent or freestanding blood collection center. The fixed site may be located in a hospital-based donor room or in a community blood center building. The site should be clean and pleasant and must meet standards of current Good Manufacturing Practices (GMP)[21] for cleanliness, ventilation, space, and temperature. Donor confidentiality must be maintained, and there must be compliance with the Health Insurance Portability and Accountability Act of 1996. Compliance with these regulations requires a screening area that provides the donor with privacy to discuss the many personal questions on the donor-screening questionnaire. There must be adequate room in the collection area for the phlebotomists to function freely, and there must be a "canteen," or refreshment area, where the donor can be orally rehydrated and observed for post-donation reactions. Properly monitored storage areas must be available for storage of blood products and equipment.

Most autologous and directed donations are performed at fixed sites. Donations that require apheresis technology, such as plateletpheresis and granulocyte collections, are also typically performed at fixed sites, although new automated blood collection technology has allowed for the collection of multiple blood products by apheresis at mobile sites as well.

Fixed sites are generally less convenient for donors than are mobile sites, as they often require additional travel, parking, and time. For this reason, a friendly, attractive, and professional staff is important. Most regular blood donors look forward to their visits and, in a sense, become part of the blood collection "family." Intensive telephone recruitment of repeat blood donors is usually necessary for a fixed site to be successful.

Plateletpheresis donations are most often collected at fixed sites. Regular plateletpheresis donors tend to differ from whole blood donors in their levels of motivation and willingness to endure longer and more uncomfortable procedures to donate their blood platelets. These donors have their blood processed by a machine for as long as 2 hours, compared to the 7 or 8 minutes needed to complete a whole blood donation. Plateletpheresis donors are able to donate more frequently (up to 24 times per year) than are whole blood donors (regular whole blood donors may only donate every 56 days). For these reasons, positive relationships between platelet donors and blood center staff appear to play a more important role in plateletpheresis donor retention. These donors are generally recruited from the ranks of repeat whole blood donors and tend to be quite steadfast and reliable.

Mobile blood drives are the ultimate in convenience for the blood donor. The donor room is essentially transported to the donor. The mobile blood collection team generally arranges mobile blood drives with a sponsoring organization, often a business, school, hospital, public service organization, religious group, or military installation. Although it is generally easier and more cost effective to run a fixed site, the convenience of a mobile drive brings many otherwise "unavailable" blood donors into the system. Once these mobile site donors have had a positive and successful blood donation experience, it is often possible to bring them to a fixed site for further donations, with effective and continuous recruitment techniques.

An adequate area must be provided by the sponsoring organization for the mobile team to set up. An experienced, well-trained collections staff is important, because everything necessary for the blood drive must be properly set up and organized on site. Essential equipment and supplies are brought by the mobile collection team, and any omission may result in cancellation of the drive or unacceptable delays. Delays and cancellations of mobile blood drives can lead to ill will between the sponsor and the blood collection center, which may dampen the likelihood of another blood drive being sponsored by that group in the future.

An alternative to using space within a school or business for a mobile blood drive is a self-contained mobile unit, usually a specially adapted bus, typically of four- to six-bed capacity. These buses are most often used for small blood drives.

Mobile blood drives should be set up along the same basic principles as fixed sites, although a certain amount of flexibility is often in order. Donor confidentiality concerns must be adhered to as best as possible, often by use of portable modular components to maintain privacy.

Recruiting for mobile blood drives requires an entirely different approach than recruiting blood donors for a fixed site. An individual from the sponsor group is often asked to organize the blood drive, by providing a personal message of support, hosting employee rallies, and designating organizers to work with a blood center representative to produce a plan for a productive and well-run blood drive. Sponsor organizers work on a personal level to recruit donors, who sign up to donate on a particular day and time. A good sponsor organizer will also do whatever is necessary to make certain each donor arrives at the appointed time. A successful drive is often followed by a recognition ceremony for all involved.

After a first successful mobile blood drive with a sponsor, future drives are generally easier to organize and run. Setting up a first-time blood drive, however, requires a blood collection center donor recruiter with excellent interpersonal and organizational skills, because it is often not a simple process to convince a sponsor to commit to a blood drive in the workplace, because of disruptions of work due to employees' taking time away from their jobs to donate blood.

Special Donations

Autologous Donation

Autologous blood donation is blood donated for the donor's own use, usually in preparation for an upcoming elective surgery. The major impetus for autologous donation is the donor's perception of eliminating the risk of transfusion-transmitted viral disease, particularly HIV and hepatitis. Recognition of transfusion-transmitted HIV in the mid-1980s greatly increased the utilization of autologous donation, which was used less frequently before that time. Another benefit of autologous donation is minimization of exposure to allogeneic red cells and leukocyte antigens that may stimulate alloantibody formation and create future transfusion compatibility problems. Some literature also suggests that allogeneic blood transfusion can lead to modulation of the recipient's immune system.[22–27]

Because the autologous donor is also the patient who will receive the donated product, deferral criteria are less stringent than for allogeneic blood donation. For example, the autologous donor can donate every 72 hours (and typically no less than 72 hours before surgery), rather than at an interval of at least 56 days. Similarly, the minimum hemoglobin level

is lowered from 12.5 to 11 g/dL for autologous donors. When multiple autologous units are requested, it is best to begin donation a few weeks in advance of the upcoming surgery. In some cases, the donor is given supplemental iron or erythropoietin injections to maintain hemoglobin levels during the autologous donation process.[28]

Collections staff who evaluate and draw autologous blood donors must have more extensive training than those who handle only routine donations. This is in part due to the fact that autologous donors tend to be older than allogeneic donors, resulting in more age-related health problems (which may thus increase the incidence of serious adverse reactions at the time of donation). The frequency of severe donor reactions requiring hospitalization, although quite low for all donors, is significantly higher among autologous donors than allogeneic donors (1 in 17,000 versus 1 in 200,000).[29] Blood center staff must also take into consideration the disease processes that made the elective surgeries necessary in the first place. Cardiac patients, for example, may have arrhythmias or symptoms of vascular disease. Orthopedic patients often have mobility problems that would adversely affect their donation experience. Blood collection staff screeners should be especially mindful of identifying those autologous donors who are at risk for ischemic heart disease, cerebrovascular disease,[30] and seizures.

The donor history form is typically abbreviated for autologous donation, insofar as risk factors for infectious disease transmission are concerned. Acceptability criteria for autologous donation often differ from routine allogeneic donation: there is a far broader list of health problems that make a donor acceptable for autologous donation that would necessitate deferral for allogeneic or routine directed donation.

Bacterial contamination of the blood product remains a risk, even for the autologous donor. Individuals with evidence of bacterial infection should be deferred from donation until the condition is resolved. Blood collection staff screeners should question the autologous donor regarding signs or symptoms of infection (e.g., fever and antibiotic use), indwelling catheters, and open wounds. Donors who have had recent procedures that could lead to a transient bacteremia, such as recent dental work or colonoscopy, are typically deferred for at least 24 hours.

Improved screening and infectious disease testing have significantly minimized the infectious disease risks of allogeneic transfusion. However, many donors and physicians continue to request autologous donation as a transfusion option. Autologous donations require more complicated donor screening and collection procedures, associated logistical problems, and associated higher costs. The autologous unit must be specifically labeled for the designated patient, and systems must be in place in both the blood center and the hospital that will guarantee that the blood arrives at the proper place, in the right condition, and in time for surgery. Occasionally, autologous blood is not available for use, due to surgery being delayed beyond the expiration of the donated blood components or due to failure of proper communication between the collection center and the hospital staff. Positive infectious disease testing or clerical errors may also delay availability of autologous blood. At the hospital, care must be taken to transfuse autologous blood before allogeneic or directed donor blood. If an adverse effect is attributed to an allogeneic or directed unit that, arguably, would never have been transfused had the autologous unit been available for use and transfused first, medicolegal consequences may ensue.

Autologous transfusion is not risk-free, so autologous units should never be transfused simply because they are available. However, individual clinicians' thresholds for transfusion of autologous blood may be somewhat lower than for allogeneic blood transfusions.[31,32] Bacterial contamination remains a risk with autologous units, and clerical errors may cause an autologous unit with positive infectious disease markers to be transfused to an unintended recipient.[33]

Excessive wastage of unused autologous blood is often an issue, because unused units are very rarely, if ever, given to other patients (i.e., "crossed over"). These units are allowed to expire at the hospital and must be discarded. "Cross-over" has been discouraged, in part, because, as a group, autologous donors have a higher frequency of infectious disease markers than regular allogeneic donors.[34] They may also have underlying disease conditions that would make them unacceptable as donors for allogeneic blood transfusion. Another factor making autologous units less desirable for allogeneic transfusion is the lower hematocrit acceptable for autologous donation, which does not meet allogeneic criteria and may provide a substandard (less potent) red cell product.

Because modern screening and testing methodologies reduce the risk of transfusion-transmitted disease, the primary medical indications for autologous donations have been reduced; however, these donations are still often medically indicated, particularly for patients who have a rare blood type. Autologous donation is also beneficial as a means of supplementing the blood supply and does provide a degree of psychological benefit to patients who fear transfusion-transmitted disease. Autologous donation may also introduce repeat donors into the system; however, the process tends not to be cost effective, as measured by traditional cost-benefit estimations.[35] Autologous donations will likely continue to decrease in popularity, unless a frightening new transfusion-transmitted pathogen, such as HIV, is discovered in the blood supply in the future.

Infectious disease testing of autologous blood and transfusion of units with positive infectious disease markers is controversial. If the blood is collected in a hospital-based donor room for use in that hospital only, infectious disease testing is not mandated. Autologous blood drawn at a community blood center, however, must be fully tested (as for allogeneic units). Autologous units positive for infectious disease must be labeled with biohazard stickers.[36,37] The AABB Standards require that if an autologus unit is to be shipped to another facility and the unit tests positive for any marker of transfusion-transmitted disease, the shipping facility shall notify the receiving trasfusion service.[38] It is the prerogative of the hospital transfusion service whether to accept autologous blood components that are positive for infectious disease(s).

Some transfusion services agree to store and transfuse autologous units that are confirmed positive for HIV, or hepatitis B or C (HBV, HCV). Evidence presented by the College of American Pathologists (CAP) indicates that many transfusion services either do not test autologous blood for infectious disease markers or knowingly collect, store, and transfuse infectious units.[39] Although transfusion of these infected units may not present an obvious risk to the donor/patient, accidental needle-sticks and splatters do put blood handlers at risk. Accidental transfusion of an infected autologous unit to the wrong recipient is possible. Storage of infectious blood components

in hospital blood banks also presents some risk to other patients, considering that at least 1 in every 25,000 blood products is transfused to the "wrong" individual.[40] In 1992, the CAP conducted a survey of 3852 hospital transfusion services and found that 34 (0.9%) had issued one or more autologous blood products to the wrong patient during the previous year, and that 20 of these units were actually transfused.[40] An analysis of 256 licensed transfusion services by The New York State Department of Health, from 1990 through 1998, indicated that 1 in 19,000 RBC units where transfused to the wrong patient or were of incorrect ABO group or Rh type.[41] In addition, preliminary data indicate the frequency of infectious disease markers among autologous donors is significantly higher than that of allogeneic donors (Table 11–2). This data, along with the decreasing benefits of autologous transfusion due to improved infectious disease testing of allogeneic blood, make the practice of storing and transfusing infected units less attractive to hospital transfusion services.

One possible reason why many transfusion services permit storage of infectious autologous units is for fear of legal action based on the Americans with Disabilities Act, which affords to asymptomatic individuals infected with HIV a protected class status.[42–46] There is a concern that not offering autologous services to these donor/patients might be interpreted as a violation of this act.[47]

Directed Donations

A directed donation is a blood donation made specifically for use by a designated patient. Directed donations are usually made by friends and family members of the patient. These donations are typically manufactured into RBCs; however, directed plateletpheresis donations are not uncommon. Using new apheresis technology, a combination of red cells and platelets (or plasma) can be donated in one sitting.

Directed donation was initially discouraged by most blood centers, for fear that the practice would institute an inequitable two-tiered blood system in which well-connected patients would have access to a safe and adequate blood supply while less fortunate patients might have none. However, the discovery of HIV in the blood supply in the early 1980s created so much demand that today directed donations have become a routine part of blood donation.

There were two schools of thought in the early days of directed donations. One suggested that individuals, under pressure to donate by friends and family members, might not be truthful about risk factors for infectious disease. These donors would, therefore, present an increased risk of infectious disease transmission to the recipient. The other way of thinking suggested that individuals would be more careful about admitting potential risk factors when making such donations. Eventually it became evident that directed donations are likely to be as safe as most first-time blood donations, but not as safe as donations from repeat donors who have a history of safe donations.[48] Although there is no evidence that directed donations are safer than routine volunteer donations, the practice often does provide a psychological sense of well-being for the patient and may alleviate the feelings of helplessness that occur when a loved one is suffering from health care problems.

Blood from directed donors is collected and tested in accordance with the same criteria that is in place for allogeneic donations and hence can be "crossed-over" and used by other patients when not required by the original intended recipient. It is the choice of the hospital transfusion service whether to utilize the practice of "crossing over." This option, however, is important to recognize, because the blood types of the donor and/or intended recipients are often not known at the time of donation; thus, incompatible directed donations are not uncommon. These units can be transfused to other patients, improving the overall blood supply. The practice of directed donation is also a valuable means of getting donors into the system, because a sizable number of these donors go on to become repeat allogeneic donors. Rather than creating a two-tiered system, as was initially feared, directed donations tend to increase the amount of blood available for all patients.

Directed donation presents a series of logistical problems not present in allogeneic donation. A physician's order must be in place indicating the number and type (e.g., platelets, RBCs) of directed units required. The blood types of the directed donors and intended recipients are often incompatible. Additionally, directed units may not be available at the time of need, because the intended directed donor was unable to donate due to fear, time constraints, or exclusionary health conditions. Fully screened and motivated donors may be unable to donate due to inadequate venous access or technical errors. Directed donations testing positive for infectious disease are discarded. For these reasons and perhaps others, directed donations may not be available for use as expected by the patient.

Communication among donors, patients, clinicians, the blood center, and the hospital transfusion service is critical

Table 11–2 **Prevalence of Donors Confirmed Positive for Transfusion-Transmitted Disease (per 10,000 donors)**

Confirmed Infection	Autologous*	Allogeneic†
HIV	3.38	0.38
HCV	110.08	8.32
HBV	13.64	3.62

HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

*Systemwide collection data from American Red Cross for calendar year 2004. Personal communication from Edward P. Notari IV, M.P.H, American Red Cross, Jerome H. Holland Laboratory, ARCNET Data Center.

†Wang B, Schreiber GB, Glynn SA, et al. Retrovirus Epidemiology Donor Study: Does prevalence of transfusion-transmissible viral infection reflect corresponding incidence in United States blood donors? Transfusion 2005;45:1089–1096.

for a successful directed donation program. A system must be in place to allow the patient and attending physician to know how many directed donor units are available for transfusion, so that more donors can be recruited if necessary. Good communication and successful procedures for directed donation programs avoid last-minute misunderstandings, in circumstances in which the anticipated number of directed units is not available when needed.

Medically Indicated Directed Donations

Directed donations are not safer than allogeneic donations, but they do increase the blood supply and provide a sense of security to the recipients. Most directed donations are not clinically necessary. However, circumstances do exist that require directed donations or in which a directed donation offers medical benefit. Using the same directed donor to provide small volumes of blood at regular intervals to neonates should reduce the risk of transfusion-transmitted diseases that would presumably be present with the use of multiple donors.[49] Similarly, one can use a small group of donors for chronically transfused patients (e.g., patients with sickle cell anemia or thalassemia).[50] Patients requiring rare blood types also benefit from specific directed donations, often from a blood relative. With proper authorization, the frequency of these medically indicated donations can be increased beyond that which would be acceptable for routine donation. In these instances, the slight potential donor risk is offset by the benefit to the recipient.

HLA-Matched Platelet Donors

Some blood collection centers test their plateletpheresis donors for human leukocyte antigen (HLA) type and store the data in a computerized database to have a readily available pool of donors to treat patients who have developed anti-HLA alloantibodies and require HLA-compatible platelets. The advent of platelet crossmatching techniques and the reduced frequency of alloimmunization, possibly due to leukoreduced blood products, have made the availability of a large HLA-typed donor pool less necessary than in previous years. However, orders for HLA-matched plateletpheresis products are still made, and most blood centers still offer this option to their hospital customers.

Donors with Hemochromatosis

Therapeutic phlebotomy is an accepted modality for preventing iron overload and subsequent organ damage for patients with hereditary hemochromatosis. Some blood collection centers, in the United States and elsewhere, have used units collected from individuals with hemochromatosis for allogeneic transfusion. These donors must meet all other allogeneic criteria. Recently the FDA has sanctioned this process by allowing variances for blood centers to collect blood from these individuals, provided certain donor follow-up and other stringent criteria are met.[51]

Donor Screening

Blood donors are carefully screened to minimize the risk of adverse consequences to the donor and to the recipient of the transfused blood. The screening process is made up of two distinct steps. The first is the donor history questionnaire (DHQ), a series of questions designed to expose potential health problems that might lead to adverse effects to the donor or blood recipient. The second step is an abbreviated physical evaluation of donor blood pressure, pulse, temperature, and venous access. The donor's hematocrit or hemoglobin levels are also evaluated at this time.

Donor screening and blood collection must be conducted under specific rules found in the CFR, as well as in applicable FDA guidelines and memoranda. In addition, the AABB, the preeminent nongovernmental organization involved with transfusion medicine in the United States, issues a publication, the *Standards for Blood Banks and Transfusion Services* (*Standards*),[52] which is adhered to by the majority of American blood centers and has been adopted into law, in varying degrees, by many states. The AABB *Standards* are upgraded regularly, to keep pace with current trends in transfusion medicine and the most recent federal regulations. Websites for the AABB (www.aabb.org) and the FDA (www.fda.gov/cber) are good sources for the most up-to-date transfusion-related regulations and information. Additionally, state and local regulations regarding blood collection practices often apply. Qualifying donor requirements, as stipulated in the most recent edition of the AABB *Standards,* are listed in Table 11–3.

Donor Identification and the Deferred Donor Registry (DDR)

Proper identification, often photographic, is required to confirm the donor's identity before donation.[53] This information is important if it becomes necessary to track down and notify the donor of any positive infectious disease test results. Proper identification is also required to perform a "lookback" study, to investigate whether a donor may have transmitted an infectious disease, unknown at the time of donation, to a blood recipient. Donors are asked if they have ever donated under any other name, possibly a maiden name or nickname, which would make it difficult to confirm previous donations. Correct personal identifiers are also necessary to calculate if adequate time has passed between donations.

Computers are becoming a mainstay of donor screening and tracking, but they can only work properly if supplied with accurate information. As an added precaution, the donor's name is compared against a database of individuals, the deferred donor registry (DDR), who have been disqualified from donating in the past, usually due to a positive infectious disease marker.[54] This database can be maintained with computers or by using manual methods such as microfiche.

During the early days of the HIV epidemic in the early and mid-1980s, the DDR was instituted as a precaution against individuals falsifying information to donate blood to obtain a free HIV test. The use of the DDR is still in effect today.

The Donor History Questionnaire (DHQ)

The donor history questionnaire is an extensive series of questions, often quite personal, designed to minimize the chance of adverse consequences to the blood donor and ensure a safe and potent blood product for the recipient. Questions are typically phrased in a "yes-no" format, other than the few open-ended questions regarding health care problems. The questionnaire must comply with requirements of the CFR and *Standards.* The AABB has developed a questionnaire that fulfills these requirements, which has been adopted, to some extent, by most blood centers in the United States (Table 11–4).[55]

A blood collection staff screener is required to answer any of the donor's questions and makes sure the forms are accurate and complete. It is crucial that the DHQ be completed properly: a false

Table 11–3 **AABB Standards Requirements for Donor Qualification***

Item	Category	Criteria
1	Age	≥17 years or applicable state law
2	Whole Blood Volume Collected	Maximum of 10.5 mL/kg of donor weight, including samples; blood collection container shall be cleared for volume collected
3	Donation Interval	8 weeks after whole blood donation (Standard 5.6.7.1 applies) 16 weeks after 2-unit red cell collection 4 weeks after infrequent plasmapheresis ≥2 days after plasma-, platelet-, or leukapheresis (see exceptions in Standard 5.5)
4	Blood Pressure	≤180 mm Hg systolic ≤100 mm Hg diastolic
5	Pulse	50–100 beats per minute, without pathologic irregularities; <50 beats per minute acceptable if an otherwise healthy athlete
6	Temperature	≤37.5°C (99.5°F) if measured orally, or equivalent if measured by another method
7	Hemoglobin/ Hematocrit	≥12.5 g/dL/≥38%; blood obtained by earlobe puncture shall not be used for this determination
8	Drug Therapy	Medication evaluation: Finasteride (Proscar, Propecia), isotretinoin (Accutane)—defer 1 month after last dose Dutasteride (Avodart)—defer for 6 months after last dose Acitretin (Soriatane)—defer for 3 years after last dose Etretinate (Tegison)—defer indefinitely Bovine insulin manufactured in UK—defer indefinitely Medications that irreversibly inhibit platelet function preclude use of the donor as sole source of platelets: Defer for 36 hours after ingestion of aspirin Defer for other medications as defined by the facility's medical director
9	Medical History	
	General health	The prospective donor shall appear to be in good health and shall be free of major organ disease (e.g., heart, liver, lungs), cancer, or abnormal bleeding tendency, unless determined eligible by the medical director. The venipuncture site shall be evaluated for lesions on the skin. Family history of Creutzfeldt-Jakob disease (CJD)—defer indefinitely†
	Pregnancy	Defer if pregnant in the last 6 weeks
	Receipt of blood, component, or other human tissue	Receipt of dura mater or pituitary growth hormone of human origin—defer indefinitely Receipt of blood, components, human tissue, or plasma-derived clotting factor concentrates—defer for 12 months
	Immunizations and vaccinations	Receipt of toxoids or synthetic or killed viral, bacterial, or rickettsial vaccines if donor is symptom-free and afebrile—no deferral [anthrax, cholera, diphtheria, hepatitis A, hepatitis B, influenza, Lyme disease, paratyphoid, pertussis, plague, pneumococcal polysaccharide, polio (Salk/injection), Rocky Mountain spotted fever, tetanus, typhoid (by injection)] Receipt of live attenuated viral and bacterial vaccines—defer for 2 weeks [measles (rubeola), mumps, polio (Sabin/oral), typhoid (oral), yellow fever] Receipt of live attenuated viral and bacterial vaccines—defer 4 weeks [German measles (rubella), chickenpox (varicella zoster)] Smallpox (refer to FDA Guidance) Receipt of other vaccines, including unlicensed vaccines—defer for 12 months unless otherwise indicated by medical director‡
	Infectious diseases	Defer indefinitely: History of viral hepatitis after 11th birthday Confirmed positive test for HBsAg Repeatedly reactive test for anti-HBc on more than one occasion Present or past clinical or laboratory evidence of infection with HCV, HTLV, or HIV or as excluded by current FDA regulations and recommendations for the prevention of HIV transmission by blood and components Donated the only unit of blood or component that resulted in the apparent transmission of hepatitis, HIV, or HTLV A history of babesiosis or Chagas disease Evidence or obvious stigmata of parenteral drug use Use of a needle to administer nonprescription drugs Donors recommended for indefinite deferral for risk of vCJD, as defined in most recent FDA Guidance 12-month deferral from the time of: Mucous membrane exposure to blood

*Reference Standard 5.4.1A- Requirements for Allogeneic Donor Qualification.

†FDA Guidance for Industry, January 9, 2002. Revised Preventative to Reduce the Possible Risk of Transmission of Creutzfeldt-Jakob disease (CJD) and variant Creutzfeldt-Jakob disease (vCJD) by Blood and Blood Products.

‡AABB Association Bulletin 05–11. Interim Standard for *Standards for Blood Banks and Transfusion Services* (23rd edition). Sept. 30, 2005.

Table 11–3 **AABB Standards Requirements for Donor Qualification—Continued**

Item	Category	Criteria
		Nonsterile skin penetration with instruments or equipment contaminated with blood or body fluids other than the donor's own. Includes tattoos or permanent makeup unless applied by a state-regulated entity with sterile needles and ink that is not re-used.
		Sexual contact with an individual with a confirmed positive test for HBsAg
		Sexual contact with an individual who is symptomatic (clinical evidence or diagnosis) for any viral hepatitis
		Sexual contact with an HCV-positive individual who has had clinically apparent hepatitis within the past 12 months
		Sexual contact with an individual with HIV infection or at high risk of HIV infection[§, ‖]
		Incarceration in a correctional institution (including juvenile detention, lockup, jail, or prison) for more than 72 consecutive hours
		Completion of therapy for treatment of syphilis or gonorrhea or a reactive screening test for syphilis in the absence of a negative confirmatory test
		History of syphilis or gonorrhea
		Other: West Nile virus—defer in accordance with FDA Guidance[#]
	Malaria	Prospective donors who have had a diagnosis of malaria or who have traveled or lived in an area where malaria is endemic and have had unexplained symptoms suggestive of malaria, shall be deferred for 3 years after becoming asymptomatic.
		Individual(s) who have lived for at least 5 consecutive years in areas where malaria is considered endemic by the Malarial Branch, Centers for Disease Control and Prevention, U.S. Department of Health and Human Services, shall be deferred for 3 years after departure from that area(s).
		Individuals who have traveled to an area where malaria is endemic shall be deferred for 12 months after departing that area.[**]
10	Travel	The prospective donor's travel history shall be evaluated for potential risks.[††]

[§]FDA Memorandum, April 23, 1992, Revised Recommendation for the Prevention of Human Immunodeficiency Virus (HIV) Transmission by Blood and Blood Products.

[‖]FDA Memorandum, December 11, 1996. Interim Recommendations for Deferral of Donors at Increased Risk for HIV-1 Group O Infection.

[#]FDA Guidance for Industry, June 2005, Assessing Donor Suitability and Blood and Blood Product Safety in Cases of Known of Suspected West Nile Virus.

[**]The Department of Defense has recommended a 24-month deferral. Department of Defense Memorandum, October 14, 1999, "Deferral of Service Members Stationed in Possible Malaria Areas in the Republic of Korea," and February 28, 2001 update.

[††] http://www.cdc.gov/travel

or missing entry must be corrected before the blood is released for transfusion. For additional clarity, screeners may be required to confirm certain critical questions verbally.[56] For autologous donors, who may have special health problems, it is often wise to have a well-trained registered nurse participate in the screening.

Other than the "yes" or "no" questions, the DHQ uses "capture questions" that cover a variety of broad topics. When an affirmative answer is given to a particular question, additional follow-up questions are asked by the screener to obtain additional information. For example, the question "Have you ever had any type of cancer, including leukemia?" often serves as a capture question that would elicit further information.

Additionally, to ensure that donors who self-administer a paper DHQ maintain focus, several "attention" questions are included. They serve to indicate if a donor is actually paying attention to the DHQ questions. The following is an example of one of the attention questions:

In the past 6 weeks, have you been pregnant or are you pregnant now? (Males check "I am male.")

An inappropriate answer to the question would be a male answering "yes" or "no." Each blood center must define the action of the screener when a donor inappropriately answers the attention questions. Attention questions may not be necessary when using other techniques to assure donor focus, such as an audiovisual computer-assisted self-interviewing system. In recent years, methods of computerized data entry have become more common.[57]

Several blood centers have investigated the use of an abbreviated donor history questionnaire (aDHQ) for repeat donors. The aDHQ eliminates nonrepeatable event questions; identifies recent changes in health, travel, or behavior; and retains questions about risk-associated activities that might have changed since the last donation. Data presented to the FDA Blood Products Advisory Committee on March 18, 2005, showed that a significant number of donors desire faster processing with a less complicated interview. This data demonstrated no indication that the abbreviated questionnaire increases blood safety risk.[58] At this time, the FDA has not accepted the aDHQ and has requested that the AABB Donor History Task Force develop a pre-implementation study of the aDHQ (currently in progress).

The minimum age for blood donation is typically age 17, but laws vary from state to state. Collections teams must follow local regulations and make certain proper consent is obtained. In some states, parental notification and/or consent may also be necessary.

Donor History Questionnaire and Donor Safety

For the majority of blood donors, the blood volume lost at donation is restored within 48 to 72 hours. With normal vascular elasticity, blood pressure is maintained and adverse reactions are kept at a minimum. Experienced screeners are more conservative with individuals who have a history of hypertension, diabetes, atherosclerosis, or other vascular diseases that can interfere with the normal physiologic response to acute blood loss, which might precipitate a hypotensive vasovagal reaction. Although rare, an acute drop in blood pressure could precipitate symptoms of otherwise occult coronary artery or cerebrovascular disease. The incidence of these disorders increases with age, so it is wise to be cautious with elderly donors or smaller donors with lesser blood volumes, for whom the acute loss of a pint of blood provides relatively more severe strain to the circulatory system.

Open-ended questions about a donor's general state of health, medications, previous surgeries, or current health care

Table 11–4 **AABB Full-Length Donor History Questionnaire, Version 1.1, June 2005***

	Yes	No	
Are you			
1. Feeling healthy and well today?	❒	❒	
2. Currently taking an antibiotic?	❒	❒	
3. Currently taking any other medication for an infection?	❒	❒	
Please read the Medication Deferral List.			
4. Are you now taking or have you ever taken any medications on the Medication Deferral List?	❒	❒	
5. Have you read the educational materials?	❒	❒	
In the past 48 hours			
6. Have you taken aspirin or anything that has aspirin in it?	❒	❒	
In the past 6 weeks			
7. Female donors: Have you been pregnant or are you pregnant now? (Males: check "I am male.")	❒	❒	❒ I am male
In the past 8 weeks have you			
8. Donated blood, platelets, or plasma?	❒	❒	
9. Had any vaccinations or other shots?	❒	❒	
10. Had contact with someone who had a smallpox vaccination?	❒	❒	
In the past 16 weeks			
11. Have you donated a double unit of red cells using an apheresis machine?	❒	❒	
In the past 12 months have you			
12. Had a blood transfusion?	❒	❒	
13. Had a transplant such as organ, tissue, or bone marrow?	❒	❒	
14. Had a graft such as bone or skin?	❒	❒	
15. Come into contact with someone else's blood?	❒	❒	
16. Had an accidental needle-stick?	❒	❒	
17. Had sexual contact with anyone who has HIV/AIDS or has had a positive test for the HIV/AIDS virus?	❒	❒	
18. Had sexual contact with a prostitute or anyone else who takes money or drugs or other payment for sex?	❒	❒	
19. Had sexual contact with anyone who has ever used needles to take drugs or steroids, or anything *not* prescribed by their doctor?	❒	❒	
20. Had sexual contact with anyone who has hemophilia or has used clotting factor concentrates?	❒	❒	
21. Female donors: Had sexual contact with a male who has ever had sexual contact with another male? (Males: check "I am male.")	❒	❒	❒ I am male
22. Had sexual contact with a person who has hepatitis?	❒	❒	
23. Lived with a person who has hepatitis?	❒	❒	
24. Had a tattoo?	❒	❒	
25. Had ear or body piercing?	❒	❒	
26. Had or been treated for syphilis or gonorrhea?	❒	❒	
27. Been in juvenile detention, lockup, jail, or prison for more than 72 hours?	❒	❒	
In the past three years have you			
28. Been outside the United States or Canada?	❒	❒	
From 1980 through 1996,			
29. Did you spend time that adds up to three (3) months or more in the United Kingdom? (Review list of countries in the UK)	❒	❒	
30. Were you a member of the U.S. military, a civilian military employee, or a dependent of a member of the U.S. military?	❒	❒	
From 1980 to the present, did you			
31. Spend time that adds up to five (5) years or more in Europe? (Review list of countries in Europe.)	❒	❒	
32. Receive a blood transfusion in the United Kingdom? (Review list of countries in the UK.)	❒	❒	
From 1977 to the present, have you			
33. Received money, drugs, or other payment for sex?	❒	❒	
34. Male donors: had sexual contact with another male, even once? (Females: check "I am female.")	❒	❒	❒ I am female
Have you EVER			
35. Had a positive test for the HIV/AIDS virus?	❒	❒	
36. Used needles to take drugs, steroids, or anything *not* prescribed by your doctor?	❒	❒	
37. Used clotting factor concentrates?	❒	❒	
38. Had hepatitis?	❒	❒	
39. Had malaria?	❒	❒	
40. Had Chagas disease?	❒	❒	

*Final Guidance from FDA not yet released on this version. Current version is 1.0 from April 23, 2004.

Table 11–4 **AABB Full-Length Donor History Questionnaire, Version 1.1, June 2005—Continued**

	Yes	No
Have you EVER—cont'd		
41. Had babesiosis?	❒	❒
42. Received a dura mater (or brain covering) graft?	❒	❒
43. Had any type of cancer, including leukemia?	❒	❒
44. Had any problems with your heart or lungs?	❒	❒
45. Had a bleeding condition or a blood disease?	❒	❒
46. Had sexual contact with anyone who was born in or lived in Africa?	❒	❒
47. Been in Africa?	❒	❒
48. Have any of your relatives had Creutzfeldt-Jakob disease?	❒	❒

problems serve to elicit potential risk factors that require careful evaluation prior to donation. Additional questions target specific medical conditions such as cardiac, lung, liver, and blood diseases; pregnancy; and cancer. A detailed discussion of the many disease states that would affect donation is beyond the scope of this chapter; however, cardiovascular disease, cerebrovascular disease, and seizure disorders are some of the primary reasons for which deferral may be indicated. Many properly controlled medical problems, such as thyroid disease, hypertension, mild seizure disorders, diabetes, and certain heart conditions, such as mitral valve prolapse, may not interfere with blood donation. It is good policy to refer difficult cases to the blood center's medical director for a final decision as to whether it is safe for the donor to donate blood. If it is not clear whether an individual meets criteria for donation, it is generally wise to err on the side of donor safety and defer the donor.

Medications are rarely of significance from the aspect of donor safety. Although angiotensin-converting enzyme inhibitors have fostered concern about potential hypotensive episodes, medications often serve to alert the screener to health problems that otherwise may have been inadvertently left out of the donor history. Use of a coronary artery dilator, for example, would indicate a history of ischemic heart disease, which might have gone unmentioned. Experienced screeners are often impressed by the lack of information that many individuals have about their own health history. Some pre-existing disease states are not mentioned by donors when completing the DHQ, as are medications and the reasons for which the medications are being taken. This may be a matter of denial or may be symptomatic of a language problem. The latter is of increasing significance as our donor population becomes more diverse.

Donor History Questionnaire and Recipient Safety

Most significantly, the DHQ exists to protect the transfusion recipient. The driving force for much of the DHQ involves screening for transfusion-transmissible infectious diseases. The greatest danger exists for diseases in which an undetected, asymptomatic carrier state exists at the time of donation. Often there are geographic or behavioral indicators that place a donor at increased risk for transmitting these diseases. The DHQ seeks to identify these risk factors to reduce the chance of disease transmission.

Viral diseases are the most tested for transfusion-transmitted pathogens. Most notorious among these is HIV, which devastated the blood supply in the early to mid 1980s. HBV and HCV (once called *non-A, non-B hepatitis*) have also caused significant morbidity and mortality in transfusion recipients. Although sophisticated infectious disease testing methodologies have significantly reduced the rate of transfusion-transmitted viral disease, the *window period* (the time during which a recently infected donor is infectious but tests negative for infectious disease markers) contributes to a low-level risk. The introduction of sensitive nucleic acid amplification technology (NAT) has shortened the window period for HCV and HIV, when compared to previous HCV and HIV antibody or HIV p24 antigen testing. However, no matter how small the risk, it is unlikely that testing will ever detect every infected blood donor, so reliance on screening cannot diminish.

Some behaviors, which have been associated with increased risk for HIV or hepatitis infection, result in indefinite deferral. These include intravenous drug use and prostitution. Male homosexual or bisexual activity, often defined as "men having sex with other men, even once, since 1977," is also considered high-risk behavior and results in indefinite deferral from allogeneic donation. Other behaviors, such as having sexual contact with a prostitute or an intravenous drug user, require a 12-month deferral from the last contact.

The DHQ is the first line of defense against such pathogens as malaria and the agents responsible for Chagas disease and Creutzfeldt-Jakob disease (CJD), for which no practical screening tests are now available in the United States.[59,60]

Donor centers should have information to indicate areas where malaria is endemic.[61] Potential donors who have traveled to an endemic area are deferred for 12 months from the date of return. Donors with a history of malaria are deferred for 3 years if symptoms do not recur.

Transmission of variant CJD (vCJD) through blood transfusion has been a controversial topic in recent years.[62,63] There has been documented disease transmission of classic CJD through dura mater grafts, pituitary-derived human growth hormone, and ineffectively sterilized electroencephalogram electrodes. Animal studies and a few reported cases in humans suggest strongly that vCJD can be transmitted by blood transfusion. Although the risk seems to be very low, the magnitude is unknown, due to the long (e.g., 30-year) incubation period. Those stricken with vCJD by eating contaminated meat products during the 1990s became symptomatic and died in just a few years.

To deal with this difficult problem, geographical screening is now in place to exclude donors who have spent time in countries where cases of vCJD have been known to occur, including the United Kingdom (UK) and much of Europe. Potential donors are indefinitely deferred who have spent a cumulative 3 months in the United Kingdom between 1980 and 1996, the period when unsafe cattle feeding practices led to an outbreak of bovine spongiform encephalopathy, or "mad cow" disease. Ingestion of infected beef at that time is believed to responsible for a number of cases of human vCJD.[64] Also indefinitely deferred are those who spent a cumulative 6 months on European military bases or a cumulative 5 years

in certain European countries other than the UK, as are those who received a blood transfusion in the UK from 1980 to the present.[65] Recipients of pituitary-derived growth hormone are deferred as are individuals with known exposure to vCJD or CJD. Until practical mass serological screening becomes available, geographical exclusions may stay in place and thousands of otherwise eligible donors will be excluded.

Exclusionary criteria are changed and updated regularly based on new threats to the blood supply. Deferral criteria may change based on improved serologic testing, and better understanding of the disease processes involved. Criteria to avoid severe acute respiratory syndrome[66] were in effect at one time, and Gulf War veterans were deferred from blood donation from 1991 to 1993 to avoid the transmission of leishmaniasis.[67–70] Donors with a history of blood-borne parasites such as babesiosis and Chagas disease are permanently deferred.

Diseases that present with severe clinical symptoms, such as hepatitis A, tend not to require special screening, because the victims are generally too sick to donate. Standards allow prospective donors who have a history of hepatitis before age 11 to be eligible for donation, provided no other cause for deferral exists.

A number of DHQ questions deal with hematologic disease, leukemia, and previous use of clotting factors. These conditions may cause abnormalities in RBCs, platelets, or plasma proteins that may lead to substandard blood products being produced.

Exposure, or even potential exposure, to another individual's blood requires a 12-month deferral. The rationale for the 12-month deferral period is that the vast majority of transfusion-transmitted infectious diseases would manifest positive serologic markers within 1 year's time. Besides blood transfusion and accidental needle-sticks, other sources of blood exposure include human bites and acupuncture, tattoos, and piercings performed with nonsterile instruments. Nonsterile body piercing (including ears) has become increasingly problematic in recent years due to the increase in popularity of piercings and tattoos. The screener should ask if the procedure was done using sterile techniques.

Vaccinations provide another area of concern for donor screening. This is particularly true for live-attenuated viral vaccines, which could theoretically infect immunocompromised individuals. Recipients of rubella and varicella zoster vaccines are deferred for 4 weeks. A 2-week deferral is required of recipients of rubeola (measles), polio (Sabin/oral), mumps, typhoid (oral), and yellow fever vaccines. Individuals vaccinated for exposure to HBV or rabies are deferred for 12 months to avoid the remote possibility of disease transmission. The American Red Cross requires a 7-day deferral period for routine (not exposure-related) HBV vaccination; the deferral time varies among different organizations. Vaccination with nonviable agents such as toxoids and nonviable antigenic material requires no deferral. Donors who are vaccinated with experimental vaccines should be carefully evaluated and deferred for at least 12 months if there is any doubt as to the safety of the agent.[71]

The September 11, 2001, terrorist attacks on the United States and subsequent attacks of anthrax, real or hoax, through the postal system created concern about bioterrorism. The United States' vulnerability to a smallpox attack resulted in plans for mass vaccinations that have caused concern in the blood banking community. Vaccination with the vaccinia virus requires a minimum of a 21-day deferral; complicated additional criteria have been established related to vaccine-related complications and whether the scab separates spontaneously. There are also deferrals for individuals who may have come in contact with a vaccine recipient. For more information, see FDA Guidance (http://www.fda.gov/cber/gdlns/smpoxdefquar.htm#iv).

Medications taken by potential donors present a significant concern for the donor screeners. Medication deferrals fall into three major categories: those that might have adverse effects on the blood recipient, those that are taken for a medical condition that might make donation unacceptable, and those that would reduce the effectiveness of a blood product.

Some drugs are teratogenic and could cause birth defects if transfused to pregnant women. These medications include finasteride (Proscar, Propecia) and isotretinoin (Accutane), each of which requires a 1-month deferral after the last dose. Leflunomide (Arava) and dutasteride (Avodart) require 3-month and 6-month deferrals, respectively. Etretinate (Tegison) requires an indefinite deferral. Drugs that might transmit infections, such as human pituitary-derived growth hormone, which is associated with CJD, are cause for indefinite deferral. In the 1980s, prior to improved screening and purification processes, hemophiliac recipients of pooled clotting factor concentrates were at very high risk for transmitting HIV and hepatitis.

Antibiotic use may indicate an active bacterial infection. Associated subclinical bacteremia may result in a contaminated blood product, which could cause serious, even fatal, consequences to the recipient.

Medications may interfere with the quality of certain blood products. This is especially true of medications that inhibit platelet function, such as aspirin. Platelet donors must have not taken aspirin within 36 hours of donation. Other medications interfering with platelet function include clopidogrel (Plavix) and ticlopidine (Ticlid).

The CFR and AABB *Standards* provide some specific guidelines with which blood collections facilities must adhere, but it is impossible to attempt to provide specific guidance for all situations. This most often becomes an issue when evaluating donors with underlying health care problems. Not only might a particular condition require medical director consideration, but often the degree of clinical severity of that condition must also be considered.[72] For example, an active case of rheumatoid arthritis may require deferral, whereas a history of rheumatoid arthritis may not. In these instances, a collection center must develop its own procedures and criteria. Although not every circumstance can be dealt with in a comprehensive manner, some centers have developed comprehensive procedures to standardize this as best as possible.[73] It is occasionally necessary, however, particularly for autologous donations, to have a properly credentialed medical director review ambiguous situations and make informed decisions on a case-by-case basis. The medical director may also be needed to resolve issues about medications, potential risk factors, and any other circumstance where a medical doctor's decision is needed.

Donor Consent and Additional Information

It is necessary to obtain informed consent prior to donation. To help ensure that the prospective donor is properly informed, educational material about the donation process is

distributed, including information about screening, phlebotomy, and potential donation-related complications. The goal of this material is for the donor to understand the reasons for self-deferral and the importance of self-deferral when appropriate. The notification process for positive serologic tests may be explained as well as donor confidentiality issues. AABB *Standards* requires review of information about the symptoms of AIDS, and the possibility of infectious disease transmission through blood transfusion. This reading material should be in language simple enough that every donor can comprehend it.[74] When local demographics demand, it may be wise to accommodate donors with materials written in a language that they can understand; otherwise, translators may be necessary. The donor must acknowledge that these materials were read and that all questions were answered.

Donor Physical Examination and Hematocrit

A brief physical examination is performed to help ensure the donor's suitability for blood donation. The physical examination consists of evaluation of the donor's pulse, blood pressure, temperature, and weight. There is also an inspection of antecubital fossae as sites of venous access.

Generally, a donor must weigh at least 110 pounds to undergo routine donation. *Standards* allows donation of 10.5 mL of whole blood for every kilogram of donor weight, but most centers purchase blood bags with a premeasured amount of anticoagulant/preservative. These have a specified minimum and maximum amount of blood that can be collected for the anticoagulant and preservatives to function according to manufacturer's specifications. For this reason, the volume of whole blood donated is fairly constant: approximately 1 pint. Assuring that the donor is of the minimum weight is important because a smaller donor, with a smaller blood volume, will suffer greater relative stress to the circulatory system. This will increase the likelihood of an adverse reaction, possibly loss of consciousness or seizures. Underweight donors are particularly likely among younger individuals, who also have a higher incidence of adverse donation reactions than older individuals.[75,76] Although the weight is generally noted from the history, it is wise to actually weigh those donors who appear to be underweight. There is no maximum weight for blood donation, but the donor's weight should not exceed the maximum capacity of the center's collection equipment.

The donor's pulse must be regular and between 50 and 100 beats per minute. A lower pulse is sometimes acceptable in athletic donors, although a medical director's approval may be necessary. A physician should also evaluate first-time donors with an irregular pulse. Allogeneic donors should be deferred if there is any question about the potential donor's cardiovascular fitness. For autologous donors with irregular heartbeats, consultation or written permission from the patient's physician may be necessary.

The donor's blood pressure must be less than 180/100 mmHg on the day of donation. First-time donors may present with elevated blood pressure due to donation-related anxiety. Allowing them a few moments' rest may lower the blood pressure to acceptable levels. Screeners should also be wary of low blood pressure in donors of small stature, advanced age, or with vascular disease, such as diabetes or atherosclerosis. These individuals may not tolerate acute blood loss as well as a normotensive donor. Blood pressure medications are acceptable if the blood pressure is controlled and the donor otherwise meets donation criteria.

The prospective donor's temperature should be less than 99.6°F. An elevated temperature may indicate a disease process that might affect the blood recipient (i.e., bacterial contamination of the product) and may require medical attention for the donor.

The potential donor's antecubital fossae are evaluated for acceptable venous access. The skin is checked for rashes, scars, or other lesions that would make phlebotomy unacceptable. The presence of "tracks" indicative of intravenous drug abuse also leads to deferral.

Determination of hemoglobin/hematocrit level is an essential part of the donation process. Whole blood collection from an anemic donor jeopardizes the donor and provides a substandard product for the transfusion recipient. *Standards* and the CFR require that donors have a minimum hemoglobin of 12.5 g/dL or hematocrit of 38% or greater.

Venous blood or finger pricks are common methods for obtaining blood for hemoglobin/hematocrit determination. Earlobe sampling, once a commonly used method, has been proven inaccurate and is not longer acceptable according to *Standards*.[77–79] Hematocrit determinations are often done using the manual microcapillary tube method or a portable point of care technology. Some facilities use the copper sulfate method, which relies on the specific gravity of blood relative to copper sulfate, to determine whether a blood sample has an adequate hemoglobin level.

Confidential Unit Exclusion

Blood donors with unacceptable risk factors for transfusion-transmitted disease might be coerced into blood donation. This situation may arise at an institutional blood drive or with directed donations for a friend or family member. The donor may deny risk factors, such as homosexuality or drug abuse, for fear that a breach of confidentiality might allow this behavior to become widely known. The confidential unit exclusion (CUE) provides the opportunity for a donor to request, with confidentiality guaranteed, that unacceptable donated blood not be used for transfusion. This procedure is accomplished by affording the donor a CUE card containing the unit number and a means of indicating, if necessary, that the unit not be used for transfusion. The CUE is then placed in a locked box to be reviewed at a later time, at which time excluded units are earmarked for destruction. In addition, centers can provide a designated telephone number so that a donor can call back with additional information, when necessary, that would exclude a unit for transfusion. When first used, the infectious disease marker frequency of units designated for nonuse by CUE was significantly higher than other units: as many as 20% of anti-HIV positive units would have been diverted from transfusion due to the CUE.[80] Improved donor education, infectious disease testing, and screening techniques have made the CUE a less valuable tool.[81–83] Many CUEs are the result of donors misunderstanding the CUE directions and inadvertently checking the wrong box.[84,85] For this reason, after investigation, some centers will destroy an excluded unit but will continue to allow the donor to donate blood.[86]

Infectious Disease Testing

Although donor screening plays an undeniable role in maintaining a safe blood supply, infectious disease testing remains

the gold standard. As of 2005, blood is routinely screened for the following disease markers:

Hepatitis B surface antigen (HBsAg)
Hepatitis B core antibody (anti-HBc)
Hepatitis C virus antibody (anti-HCV)
HIV-1 and HIV-2 antibody (anti-HIV-1 and anti-HIV-2)
HTLV-I and HTLV-II antibody (anti-HTLV-I and anti-HTLV-II)
Nucleic acid amplification testing (NAT) for HIV-1 and HCV
NAT for West Nile virus (WNV)
Serologic test for syphilis

Although hepatitis plagued the blood supply for many years, it was not until the mid-1980s and the discovery that HIV was transmitted through blood transfusion that blood safety became a national obsession. Currently, the risk of transfusion-transmitted HIV may be as low as 1 in 2 million units.[87] Despite this, HIV is the most feared transfusion-transmitted disease.

Risk of HBV contamination may be as low as 1 in 100,000. NAT testing for HBV is still not in widespread use, although it is under consideration.[88,89] The debate, in part, consists of whether it is more cost effective to spend public funds on HBV vaccination programs or for NAT testing of the blood supply, and whether NAT testing would be more sensitive for "window period" detection of donors who have lost HBV antigenemia.[90,91]

The anti-HBc test is somewhat controversial.[92] It was once considered a surrogate marker for HIV, but improved serologic testing for HIV would seem to make anti-HBc unnecessary. The high false-positive rate for this marker further limits its usefulness. However, its proponents suggest that anti-HBc detects those donors who remain infectious of HBV who have lost HBsAg positivity.

Hepatitis C virus was once considered responsible for a transfusion-transmitted hepatitis rate of up to 10%. Current estimates of HCV transmission may be as low as 1 in 2 million units.

The test for antibodies to HTLV is also controversial.[93] Early on, HTLV-II was considered a possible etiologic agent of hairy-cell leukemia. This has been proven not to be the case, and HTLV-II is currently not associated with any disease process. HTLV-I is associated with adult T-cell leukemia/lymphoma in Japan and HTLV-associated myelopathy and tropical spastic paraparesis, chronic demyelinating diseases found in the Caribbean. The confirmatory test for HTLV is often time consuming and expensive. Many screening test results are not confirmed, however; the donated blood is destroyed and the donor is alarmed for no apparent reason.[94] Because HTLV-associated diseases are highly unusual in the United States, the necessity of HTLV as a screening test is unclear.

The most recent threat to the blood supply is West Nile virus. WNV is a mosquito-borne pathogen known to cause meningoencephalitis. Once it was recognized as a threat to the blood supply in 2003, NAT became available in fairly short order. In 2005, WNV seems to be an increasing threat, but the highly successful screening program has reduced its transmission by transfusion significantly.

Serologic testing for syphilis is another somewhat controversial test because transfusion-related transmission of this disease has been documented only recently. Some consider it to have value as an indicator of lifestyle problems that might make blood donation undesirable.

Collection

Prevenipuncture Procedures

The collection process begins with accurate identification of the blood donor. This is especially important in large centers where screening and phlebotomy are done in separate areas and by different staff. A unique identification number is placed on the collection bags, paperwork, and the pilot tubes collected for serologic testing. The phlebotomist applies mild pressure over the upper arm, usually with a blood pressure cuff or tourniquet. The increased venous pressure engorges the veins in the anticubital fossa, making them easier to detect for phlebotomy. Once a vein is selected, the skin is thoroughly disinfected, often using a two-step procedure utilizing soap and iodine solutions.[95] After the skin has been disinfected, the phlebotomist performs the venipuncture and the collection begins.

Whole Blood Collection

Whole blood is collected by means of venous pressure and gravity. Usually, the phlebotomy needle comes attached to a preconfigured bag system containing a premeasured amount of anticoagulant and preservative. A number of different anticoagulant/preservative preparations are available. The maximum liquid storage time for any RBC unit is currently 42 days. The number of bags in the collection set depends on intentions for further manufacture: whole blood, packed cells and plasma, or packed cells, plasma, and platelets. Multiple small bags can be attached if the blood is designated for pediatric transfusion. It is possible, through a sterile docking device, to add additional bags to a set. It is also possible to manually adjust the amount of anticoagulant in a collection bag for an underweight donor, but this requires significant time and expertise and is not done in most centers.

The collection bag is often placed on a trip-scale, which impedes further blood flow once the desired amount (usually 450 or 500 mL) has been drawn. The blood is agitated during collection, either manually or with an automated device, to ensure adequate mixing with the anticoagulant-preservative mixture in the bag. Many facilities choose to utilize a blood collection system that diverts the initial aliquot of donor blood into an integrally connected pouch. This diversion reduces the possibility that a skin plug or core cut with the needle during phlebotomy, possibly harboring bacteria, will contaminate the collection bag. Blood in the diversion pouch can be used for blood typing and viral marker testing without increasing blood loss associated with donation. This technique (diversion pouch) may reduce bacterial contamination rates in blood components overall by about 40%, with the highest reduction observed for common skin contaminants.[96,97]

Apheresis Platelet Collections

Plateletpheresis is a sophisticated technology by which blood is processed by an apheresis machine that uses centrifugation to remove a selected component of the blood and returns the rest to the donor. The most common use of this technology is for collection of apheresis platelets. Platelet donors are usually recruited from the ranks of whole blood donors. The minimum platelet count required to donate apheresis platelets is 150,000/μL. Apheresis platelet donors can donate more frequently than whole blood donors: AABB *Standards* limits apheresis platelet donations to no more than twice in a 7-day period and no more than 24 times per year. The apheresis procedure is more rigor-

ous than whole blood collection because the donor must remain connected to the apheresis machine for an extended period, often 1 to 2 hours. Another difficulty is the high incidence of hypocalcemic reactions, due to the calcium-binding anticoagulant used to keep blood from clotting in the machine.

Platelets collected through apheresis technology have some advantages over random donor platelets (RDPs, collected by centrifugation from individual whole blood units) because 1 apheresis platelet unit is the equivalent of 6 to 10 RDPs. This decreases the risk of transfusion-transmitted disease and allergic transfusion reactions. If an apheresis donor's platelet count (and patience) is sufficient, a double or even triple product can be collected at one sitting. Many apheresis platelet technologies provide a leukocyte-reduced product.

Granulocytapheresis

Granulocytapheresis produces a product of concentrated neutrophils using apheresis technology. Granulocytes are used to treat neutropenic patients with infections that are not responding to antibiotics. Donors are placed on an apheresis machine with granulocytapheresis capabilities. Not all machines can perform granulocytapheresis: many of the newer machines are specialized for collection of platelets or plasma. The machine must be properly programmed and the operator specially trained for granulocyte collections.

A significant challenge to granulocytapheresis therapy is collecting enough granulocytes to produce a therapeutic response. Granulocytapheresis donors are premedicated with corticosteroids and/or granulocyte-colony stimulating factor (G-CSF) before collection, to maximize granulocyte yield. These medications cause release of marginated granulocytes from the spleen and major blood vessels, markedly increasing the peripheral blood granulocyte count before donation.[98] Higher peripheral granulocyte blood counts result in larger granulocyte collections.

Regimens for premedication vary. An example dosage is 5 to 10 μg/kg administered subcutaneously, 12 hours before the collection procedure. It is recommended that one consult the manufacturer's package insert for specific dosage guidelines.[99–101] Corticosteroids are usually given as prednisone or dexamethasone. The latter is given as a dose of 8 to 12 mg, depending on the donor's weight, at intervals of 4 and 12 hours before the collection procedure. A uniform dose of 450 μg of G-CSF coupled with 8 mg of dexamethasone, both given 12 hours before collection, has been shown to be as effective as larger combined doses.[102]

Producing a granulocytapheresis product that is not heavily contaminated with RBCs has also been a challenge. The density of granulocytes is only slightly lower than that of RBCs, which makes it difficult to produce a clean separation. RBCs in the granulocyte product must be compatible with the recipient to avoid the possibility of an acute hemolytic transfusion reaction. To help remedy the problem of red cell contamination, differential sedimentation is enhanced by use of rouleaux-inducing agents. Both hetastarch and pentastarch are employed for this purpose, although hetastarch is more widely used for its higher granulocyte yields.[103] Hetastarch, however, is less rapidly cleared from the body and accumulates more readily in the extravascular space, which can lead to localized edema, headache, and fluid retention in repeat donors, often family members, who donate regularly over a period of several days. It may be wise to use reduced dosages for frequent donors to help avoid these effects. These adverse effects tend to be less of a problem for infrequent donors and with collections using pentastarch. Although traces of hetastarch may be detected in the donor for years, there has been no demonstrated clinical significance. Combined premedication with G-CSF, dexamethasone, and collection with the use of hetastarch have been reported to provide a product with a granulocyte yield of 4.1 to 10.8×10^{10} compared to 2.1 to 2.6×10^{10} using dexamethasone alone.[104]

Granulocytapheresis products should be administered at least daily to an adult patient to achieve a physiologic dose, and this must be repeated for a number days. This requirement creates serious logistical problems and is one reason why (along with the cost) granulocytapheresis is not more frequently utilized. Improved antibiotic therapy and the high incidence of adverse effects in the recipients of granulocytapheresis products, including pulmonary reactions and leukocyte alloimmunization, have further decreased the functionality of this therapy.[105,106]

Hematopoietic Progenitor Cells, Apheresis

Collection of hematopoietic progenitor cells by apheresis (HPC-A), often referred to as *peripheral blood stem cells* or *stem cells,* has become increasingly prevalent over the past decade. The main advantage of HPC-A over hematopoietic progenitor cells, marrow (HPC-M) is that adequate HPC-A can be collected to support several courses of high-dose chemotherapy. Furthermore, transplantation of autologous HPC-A results in a more rapid hematopoietic recovery compared to autologous HPC-M. HPCs are mobilized into the donor's peripheral blood from the bone marrow with the use of recombinant colony-stimulating factors, either G-CSF, granulocyte-macrophage colony-stimulating factor, or a combination of the two.

Autologous HPC-A collections may be performed following, without, or in conjunction with chemotherapy. Apheresis is performed for several days as necessary, until an adequate stem cell dose is achieved. The adequacy is determined by the CD34+ dose (the number of CD34+ cells per kilogram of recipient body weight). It is generally agreed that a minimum dose of 2.5×10^6/kg CD34+ cells is necessary for successful engraftment.[107] In most autologous collections, venous access is obtained through a dual- or triple-lumen catheter.

Collection of allogeneic HPC-A from HLA-matched relatives is primarily performed using G-CSF mobilization. Clinical trials have suggested that a dose of 2.0×10^6/kg CD34+ cells is a minimum threshold for transplantation.[108]

Collections of HPC-A can be stored unmodified or can be processed further with the intent of improving outcomes. These include purging of cancer cells utilizing monoclonal antibodies,[109] CD34+ selection techniques,[110] and ex vivo expansion[111] (i.e., culture techniques).

Plasmapheresis

Most plasma for transfusion is produced by centrifugation of a unit of whole blood, which produces a unit of platelet-rich plasma and a unit of RBCs. Plasma can also be obtained using apheresis technology. Apheresis plasma is usually collected from group AB donors, which is of particular value because it can be transfused to patients with any blood type, although several investigators have raised concerns regarding the impact of ABO nonidentical blood product transfusions on patient outcomes.[112] The advantage of apheresis plasma

technology is the ability to collect larger units, often called *jumbo plasma*. Larger units are desirable because fewer units are required per dose, which lessens the chance of infectious disease transmission and allergic reactions per recipient. For blood centers collecting blood for transfusion, plasma collections usually occur at an interval of 4 weeks or greater and must be compliant with FDA guidelines for "infrequent plasmapheresis."[113] These donors must meet whole blood criteria and are limited to an annual maximum of 12 L of plasma (14.4 L if at least 80 kg).

"Source" plasma is collected in large quantities by commercial firms for fractionation into plasma derivatives used to produce reagents and other plasma products. Source plasma is not for direct human transfusion. Because source plasma donors are often paid and tend to be aggressively recruited, specific regulatory requirements have been designed to protect the frequent plasmapheresis donor. These donors can donate a maximum of twice in a 7-day period, with at least 2 days between donations. Frequent donors require periodic physical examination by a physician and periodic determination of serum protein levels.

Multiple Apheresis Products

New apheresis technologies now make possible the collection of multiple products in a single donation when appropriate donor criteria are met. A double red cell product can be collected every 16 weeks if the donor meets the specified weight and hematocrit criteria. Some donors appreciate the convenience of donating less frequently. The collection of multiple products from a single donation helps to maintain an adequate blood supply and is often more cost efficient for the collection facility.

Adverse Donor Reactions and Injuries

The vasovagal reaction is the most common systemic donor reaction, occurring in 2% to 3% of donors.[114–117] These reactions often present as loss of consciousness due to a drop in blood pressure without a normal compensatory increase in heart rate. Vasovagal reactions are 5 to 10 times more frequent in younger donors (8% to 11%),[118] making careful observation especially important at high school and college blood drives. Other predisposing factors include first-time donor status,[119] low weight,[120] and a history of a previous donation reaction.[121,122] An anxiety-related psychosomatic component appears to be present because vasovagal reactions have occurred before donation and epidemic fainting is known to occur.

Vasovagal reactions often occur with short warning, during or immediately or after phlebotomy. Experienced phlebotomists know to look for lightheadedness, weakness, pallor, nausea, and diaphoresis. Excessive anxiety, often manifested by nervous talkativeness and hyperventilation, can precipitate a vasovagal reaction. Hyperventilation can result in respiratory alkalosis and hypocalcemia, which can help precipitate a vasovagal reaction.[123] In these instances, having the donor breathe into a paper bag may increase carbon dioxide levels, reversing the alkalosis and hypocalcemia. A calm, assuring demeanor by the phlebotomist will also do much to alleviate anxiety.

Approximately 5% of vasovagal reactions are syncopal and progress to loss of consciousness in about 0.08% to 0.34% of donors.[124] Syncopal reactions tend to occur after phlebotomy—about 60% occur at the refreshment table and 12% occur after the donor has left the collection site. This underscores the importance of closely observing donors even after the donation has been completed without incident. From 30% to 45% of the syncopal reactions include involuntary tetany or tonic-clonic convulsive movements.[125] These usually last less than 30 seconds; however, 20% may last longer, up to a minute or two. These can also progress to full-blown tonic-clonic seizures with associated urine incontinence. Prolonged hyperventilation can rarely lead to tetany without syncope as a result of hypocapnea leading to hypocalcemia. Severe vasovagal reactions may resemble shock clinically, except that the pulse is slow rather than fast. When the blood pressure becomes extremely low the donor often becomes pale and even cyanotic.

Mild vasovagal reactions are treated by elevating the donor's legs above his or her heart, helping to improve blood flow to the brain. Ammonium salts, cold neck compresses, and reassurance are often all that is necessary, and the donation can proceed. Treatment with intravenous fluids or medications is usually unnecessary if the donor does not have an underlying medical condition such as coronary artery or cerebrovascular disease. Experienced staff can help avoid a severe vasovagal reaction by recognizing and treating a reaction in the early stages.[126,127] Treatment of more severe vasovagal reactions, which may proceed to loss of consciousness and seizure activity, require that the donation be stopped and the needle be withdrawn to prevent local tissue injury from convulsive movements. The main risk associated with syncopal vasovagal reaction is trauma, particularly head trauma. Fractures and other significant injuries have been reported.[114] Some centers keep tongue protectors available, but damage to the tongue from convulsive movements is rare. The typical time for recovery from a vasovagal reaction is 5 to 30 minutes.

On occasion, a particularly severe reaction may require additional resources. Hospital-based donor rooms may have access to an emergency response team with a crash cart to deal with these situations. For remote centers without an onsite emergency response team, it may be prudent to call paramedics and have the donor transferred to a local emergency room if necessary. Maintaining a crash cart in the donor center with emergency life support equipment and medications is controversial. Centers that rarely see a severe reaction may have little or no actual experience with advanced life support procedures despite formal accreditation and may be unfamiliar with the available emergency equipment when needed. It may be better to have an emergency backup system, often calling 911, than to have an crash cart and not know how to use it.

Vasovagal reactions may recur within the next several hours and so donors who have had one should be advised to use caution when driving or operating heavy machinery. Donors with severe or multiple reactions should be discouraged from attempting to give blood again in the near future. Even donors who have had severe vasovagal reactions tend to recover spontaneously. No reports of deaths caused by blood donation-related vasovagal reaction appear in the medical literature, although there are reports of cardiac arrest in patients after venipuncture for blood sample collection.[128,129]

The sudden drop in blood pressure caused by a vasovagal reaction may evoke an ischemic event in donors with occlusive atherosclerotic vascular disease. These reactions tend to be rare, likely due to successful donor screening techniques.[114] The risk, of course, is higher for individuals with pre-existing

disease, so these donors should be accepted only if their disease is stable and even then with caution. Some degree of risk may be acceptable for autologous donation, which is commonplace for elective cardiac bypass surgery (if the patient does not have unstable angina).[30,130] Taking chances with a routine allogeneic donor is unacceptable, and if there is any real uncertainty, the donor should be deferred.

Cerebrovascular disease presents a special problem because loss of consciousness and mild seizure activity may be manifestations of both a vasovagal reaction and cerebrovascular ischemia. For a donor with a known history of cerebrovascular disease, distinguishing a donation reaction from a stroke or transient ischemic attack may be difficult. For the same reasons, it is generally a good idea to be cautious about accepting a donor with a poorly controlled seizure disorder.

Minor local tissue injury at the venipuncture site is a well-known complication of any venipuncuture. Postphlebotomy bruising is the most common adverse donor event. Two studies of outpatient phlebotomy suggest that the incidence of bruising may range from 9% to 16%.[131,132] Hematomas occur less commonly: approximately 0.3% at the time of donation and an additional 0.05% reported by the donor later. Hematomas, bruising, and soreness can usually be treated with compresses and acetaminophen. These hematomas generally resolve within 2 weeks.

Accidental arterial punctures are rare.[125] They may present as an unusually rapid phlebotomy with bright red blood and a pulsating needle. On recognition, the phlebotomy should be stopped and pressure should be applied for at least 10 minutes. The donor should be closely observed for an extended period. If there is any question about effective hemostasis, competent medical consultation should be obtained. Brachial artery pseudoaneurysm,[133,134] arteriovenous fistula,[135] and compartment syndrome[136] are possible sequelae of arterial puncture. All three complications are rare but do require surgical repair.

Nerve damage due to a hematoma or direct trauma is an unusual event. Reports suggestive of nerve damage occur in approximately 1 of every 6000 blood donors.[137,138] Symptoms may include pain and paresthesias at the venipuncture site extending into the donor's hand, fingers, or shoulder area. A hematoma is present in approximately 25% of cases. Approximately 40% recover in a few days and 70% recover completely within 30 days. The remaining 30% take as long as 9 months to recover. A few donors have a small area of persistent numbness even after 9 months. Rarely, significant permanent neurologic damage occurs.

Bactericidal skin cleansing solutions and adhesive tape can cause local allergic reactions and irritation despite extensive prerelease testing and FDA approval. For iodine-sensitive donors, alternative solutions can be used. Post-donation hemostasis can be attained with pressure dressings rather than adhesive tape.

A common adverse effect of apheresis donation is hypocalcemia, due to the calcium-binding citrate anticoagulant used to keep blood from clotting in the apheresis machine tubing. Return of citrated blood to the donor may cause lightheadedness and perioral and peripheral paresthesias. These are readily treated by ingestion of calcium-containing antacid tablets. On machines that allow more extensive operator control, the rate of citrate infusion can be lowered to help diminish these reactions.

Apheresis removes a limited amount of blood from the donor at any given time, so vasovagal reactions and other adverse effects precipitated by acute volume loss are less pronounced. The two-needle continuous flow technology draws blood from one vein at the same rate as processed blood is returned in the other. Intermittent single-needle technology removes and replaces blood in very small increments. The decreased rate of vasovagal reactions among apheresis donors may also be due to the fact that these donors tend to be older and more experienced with the donation process. As with whole blood donation, the frequency of adverse reactions is higher in first-time apheresis donors. Vasovagal reactions, for instance, range from 2.0% in first-time to 0.5% in repeat donations.

Other than mild citrate reactions, adverse events are seen with an overall frequency of 2.18% (428 of 19,611 donations from 17 centers).[139] The most common adverse events are related to the venipuncture, with a frequency of 1.30%. Palpable hematoma accounted for 88% of these events. The risk of a hematoma is higher for a plateletpheresis procedure than for a whole blood donation (0.3% for the latter; Table 11-5). This may be due to the extended time frame that the needle is in place compared with the 10 to 15 minutes for a whole blood collection.

Other adverse effects of apheresis include RBC hemolysis, air emboli, clots, and leaks. These have been reported but are extremely rare with improved apheresis technology and better-trained operators. The incidence of adverse apheresis reactions varies among institutions, which may be due to donor selection, operator training, or even record keeping. One program has reported an overall 0.81% frequency of adverse events; of 19,736 procedures, 47 (0.24%) were rated as serious.[140] Seven of these 47 donors required transfer to an emergency department.

A single unit plateletpheresis procedure will cause a drop in the donor's platelet count of approximately 30,000 to 50,000 platelets/μL, although a return to prepheresis levels will usually occur in a few days.[141,142] In some donors, frequent plateletpheresis may cause a gradual drop in platelets, such that collections must be discontinued, or possibly donations can be scheduled with longer intervals between donations.[143] The platelet count usually recovers in these donors over several months without treatment. Donors with persistent thrombocytopenia are deferred from platelet donation.

Lymphocytes, which have a density similar to platelets, are often lost during a plateletpheresis procedure. In theory, frequent plateletpheresis could remove enough lymphocytes, especially long-lived T lymphocytes, to cause immune dysfunction. At this time, however, no adverse clinical effects have been observed in healthy donors.[144]

The same adverse effects of plateletpheresis are also be seen with granulocytapheresis. In addition, the sedimenting agents used to effectively remove granulocytes and the medications used to stimulate the donors' granulocyte counts have additional side effects. Small doses of corticocosteroids have been reported to cause insomnia in up to 25% of donors.[145] Frequent granulocyte donors should be free of peptic ulcers, diabetes mellitus, hypertension, glaucoma, and other diseases exacerbated by prolonged use of corticosteroids. A combined dose of G-CSF and dexamethasone may cause side effects in as many as 72% of donors; these are commonly insomnia (30%), mild bone pain (41%), and headaches (30%). The latter two are readily relieved by analgesics.[146] Sedimentation agents, usually hetastarch, may cause fluid retention and allergic reactions.

Table 11–5 **The Incidence of Whole-Blood Donor Complications and of outside Medical Care**

Variable	Incidence: Observation/ Donor Complaints[†],%	Incidence: Observation and Postdonation Interview[‡], %	Outside Medical Care Reported to American Red Cross in 2003[§] (cases per 10,000)
Arm injuries			
Bruise	NA	22.7	See hematoma
Sore arm	NA	10.0	Unknown
Hematoma	0.35	1.7	0.57 (1/17,500)
Nerve irritation	0.02	0.9	0.46 (1/21,700)
Local allergy	0.5 (estimate)	NA	Unknown
Arterial puncture	0.01	NA	0.07 (1/142,900)
Thrombophlebitis	0.002 (estimate)	NA	0.01 (1/75,000)
Thrombosis	Very rare	NA	<0.001
Local infection	0.002 (estimate)	NA	<0.01 (1/225,000)
Systemic			
Fatigue	NA	7.8	Unknown
Vasovagal reaction	2.5	7.0	1.08 (1/9300)
Syncope	0.08–0.34	NA	See above
Syncope with injury	0.01–0.05	NA	See above
Nausea, vomiting	NA	0.4	Unknown
MI, stroke, etc.	Very rare	Very rare	Unknown
Total (donors)	3.5	37	2.94 (1/3400)[‖]

[‖]MI, myocardial infarction; NA, not applicable.

From Newman BH. Blood donor complications after whole-blood donation. Curr Opin Hematol 2004;Sep;11(5):339–345.

[†] Newman BH. Donor reactions and injuries from whole-blood donation. Transfusion Med Rev 1997;11:64–75.

[‡]Newman BH, Pichette S, Pichette D, et al. Adverse effect in blood donors after whole-blood donation: a study of 1,000 blood donors interviewed 3 weeks after whole-blood donation. Transfusion 2003;43:598–603.

[§]Newman B, Crooks N, Zhou L, et al. Whole-blood donor complications leading to outside medical care: National overview and a detailed review at one blood center [abstract]. Transfusion 2004;44(Suppl):77A.

[‖]Includes an unlisted category of "other."

Post-Donation Procedures

When the collection is complete, the tubing between the donor and the collection bag is clamped to stop the blood flow. Typically, pilot tubes for serologic testing are filled according to procedure, and the needle is removed. A pressure dressing is applied to the venipucture site to achieve hemostasis. When the bleeding is stopped, a bandage is generally applied and the donor is escorted to a refreshment area.

Blood remaining in the collection tubing is "stripped" into the collection bag to ensure adequate mixing with the anticoagulant/preservative solution. Refilled tubing is sealed into individual attached segments to be used for compatibility testing at a later time. The unit is then documented, stored, and transported to its next stop according to procedure.

The donor must remain in the canteen area under observation for approximately 15 minutes to ensure that the staff can quickly react should a reaction occur. Liquids are given to help replace those removed during the donation procedure.

The donor should receive a post-donation packet that includes information about caring for the venipuncture site, drinking liquids, and describes appropriate post-donation activity levels. A telephone number is provided to call if the donor has an adverse reaction or wishes to modify the health history information. Once stable, the donor can be released and possibly scheduled for the next donation.

Safety Concerns

Safety is always a concern when working with biohazardous materials. Safety issues have come under increasing regulatory surveillance, and there is particular concern about accidental exposure through used needles, lancets, and microhematocrit tubes.[147] Retractable needle covers to avoid accidental needle-sticks have become mandatory in some states. Safety devices are also available for filling pilot tubes. Disposable lancets and glass microhematocrit tubes can puncture skin if not handled properly. Proper disposal of used needles, lancets, and microcapillary hematocrit tubes in specialized "sharps" containers is mandatory. A properly designed and enforced Exposure Control Plan is a key element in preventing occupational blood exposures and transmission of blood-borne pathogens.

Although volunteer blood donors have a low prevalence of transfusion-transmitted disease,[148] use of disposable gloves should be encouraged, especially for staff with open wounds on exposed skin.[149] If a staff member is exposed, the employee should be counseled immediately and offered postexposure testing and prophylaxis for HIV infection.[150] Postexposure prophylaxis (PEP) should begin within 2 hours of exposure, so it may not be possible to delay treatment until infectious disease testing results on the donor are available. Although PEP for potential HIV transmission should be offered, its use is not justified for exposures that pose a negligible risk.[151,152] PEP, if taken, should be discontinued if the source is later determined to be HIV negative. Rapid testing of HIV of source donors or patients can facilitate making timely decisions regarding the use of HIV PEP.

Treatment for exposure to other transfusion-transmitted diseases is less time sensitive and can usually wait until testing of the donor in complete. If the donor is found to be HBsAg positive, a nonimmune staff member should be offered hepatitis B immune globulin within 7 days of exposure and HBV vaccine.[153] It is recommended that staff receive the HBV vaccine on initial employment, unless one is prohibited from receiving the vaccine for medical reasons or is otherwise already immune.

Table 11–6 **Example of Causes for Lookback Notification**

Item	Lookback Initiated If
HBsAg	Repeatedly reactive HBsAg confirmed positive by neutralization (or neutralization not done) is found in a subsequent donation whose prior test results were nonreactive **OR** Repeatedly reactive HBsAg, negative neutralization AND repeatedly reactive HBcore is found in a subsequent donation whose prior test results were nonreactive
HBcore	Repeatedly reactive anti-HBcore, and the test result of the second test method is reactive in a subsequent donation whose prior test results were nonreactive **OR** Repeatedly reactive anti-HBcore and repeatedly reactive HBsAg in a subsequent donation whose prior test results were nonreactive
HTLV-I/II	Repeatedly reactive anti-HTLV-I/II and the second test result is repeatedly reactive or not performed is found in a subsequent donation, whose prior test results were nonreactive or not previously tested
Anti-HIV-1,2	Repeatedly reactive anti-HIV-1,2 confirmed positive HIV-1 Western Blot **OR** HIV-2 EIA reactive found in a subsequent donation not previously tested or whose prior test results were nonreactive
HIV-1 NAT	NAT reactive AND HIV-1 Western Blot (or IFA) indeterminate positive or HIV-2 EIA reactive is found in a subsequent donation whose prior test results were nonreactive or prior donation was not tested
Anti-HCV	Repeatedly reactive anti-HCV with a supplemental test result of positive, indeterminate OR no supplemental test performed found in a subsequent donation whose prior donation was not previously tested with the currently licensed test, or whose prior test results were nonreactive
HCV NAT	NAT reactive with a supplemental test result of positive, indeterminate OR no supplemental test performed found in a subsequent donation whose prior donation was not previously tested, or whose prior test results were nonreactive
WNV	Current donation sample has a reactive WNV NAT. Relevant collections include those occurring between 120 days prior to the date of the reactive test and 120 days after the date of the reactive test. Donor reports a diagnosis of West Nile virus occurring between 14 days prior to the onset of illness and up to and including 120 days subsequent to the onset of illness or diagnosis, whichever is the later date. Donor reports unexplained febrile illness with headache or symptoms suggestive of WNV infection between June 1 and November 30, and Medical Director has determined this represents likely infection by WNV. A report is received regarding possible transmission of WNV by a blood component received within the 120 days prior to the onset of symptoms, or a WNV- fatality in a transfused recipient. Prompt quarantine and retrieval for in-date components collected from the donor of suspect donation in the period between 120 days before the suspect donation and up to and including 120 days after the suspect donation must be performed.
CJD or vCJD Risk factors	Subsequent to donation, the donor: is diagnosed with Creutzfeldt-Jakob disease indicates a family history of Creutzfeldt-Jakob disease acknowledges receipt of human pituitary-derived growth hormone (HGH) acknowledges receipt of a dura mater transplant indicates having spent a total time of 3 months or more in the United Kingdom from 1980 through 1996 indicates receipt of injectable products from cattle in BSE-endemic countries acknowledges spending a total time of 5 years or more in Europe, including time spent in the UK If a member of the U.S. military, a civilian military employee or a dependent of a member of the US military and spent a total of 6 months or more associated with a military base in any of the following countries: From 1980 through 1990 in Belgium, the Netherlands, or Germany From 1980 through 1996 in Spain, Portugal, Turkey, Italy, or Greece
AIDS-related	If a donor implicated in the investigation of transfusion-associated AIDS has a reactive test result for anti-HIV-1, 2 and/or HIV-1 antigen. If information is received that a patient with AIDS has previously donated blood.
High-risk behavior (e.g., travel, vaccination malaria, tattoo, blood exposure)	Post-donation information becomes available regarding a donor who would have been deferred had the information been known at the time of donation.

Compliance Issues

The management of unexpected events may often be referred to as *error* or *deviation management*. Because humans are fallible, limiting the incidence of errors to absolute zero can never be achieved.[154, 155] Well-prepared organizations approach error management from a systems level, anticipating that errors and deviations will occur, and prepare system defenses for dealing with their inevitable occurrence rather than focusing on blaming individuals for forgetfulness or inattention.[154]

Lookbacks

Being human, blood donors themselves represent a source of deviation. With the incubation time between exposure and onset of disease, some individuals are unaware that they may be infectious to others. To identify these individuals, a donor center must develop procedures to notify the recipients of blood or components of previous donations when a donor becomes confirmed positive for an infectious disease marker, or when a statement of high-risk information dis closed at a subsequent time determines that the donor was actually ineligible at the time of their donation. Identification of persons who may have received blood or components from such donors is referred to as *lookback*. Examples of causes for lookback may be seen in Table 11–6.

On identification of a unit meeting lookback criteria, a facility must search records for prior donations by the same individual. A sample worksheet may be seen in Figure 11–1. The highest priority should be placed on the most recently donated units. This should be done within 72 hours, so that any unit(s) remaining in inventory may be immediately quarantined. Policies must include consignee notification, so that any components shipped to other facilities may be immediately quarantined and returned. A sample notification letter and product disposition record may be seen in Figures 11–2 and 11–3.

If the implicated donor has donated on many occasions, lookback notification should be started with the most recent recipients. Reasonable and timely attempts must be made to notify transfusion recipients, particularly if a lookback is due to HIV[156] or HCV,[157] so that recipients may obtain testing, counseling, and medical referral as needed.

Recalls and Market Withdrawals

Errors can also result from improper testing, incorrect labeling of components, improperly interpreting test results, improperly using equipment, or failure to follow the manufacturers' directions or facility procedures. These kinds of errors may result in recalls or market withdrawals.

Recalls are defined as actions taken by a facility to remove a product from the market.[158,159] Recalls may be conducted

Somewhere Donor Center
Anywhere, State, Zip

LOOKBACK WORKSHEET **Case Number:** _____

Unit Number			Unit # of						
Date/Time Initiated			By:						
Unit collected by (facitlity name)									
Notified by (name, date, time)									
Components prepared/received (✓)	Unit status (INV, QU, TF, DS, or SHIP)	**If in Inventory,** Quarantined Date/Time	**If Shipped** Date Shipped	Consignee Name	Consignee Notified Date/Time/By	Consignee Contact Name	**If Transfused** Patient Name	Medical Record Number	Patient Status
❑ Whole Blood									
❑ Red Cells									
❑ Fresh Frozen Plasma									
❑ Platelets									
❑ Recovered Plasma									
❑ Cryoprecipitate									
❑									
❑									
❑									

FOR USE BY COMPLIANCE:

Other information (Patient primary physician notifications, final outcomes, response from consignees). List by component. Use other side as necessary and attach all related documents.

Unit Status Legend: INV = Inventory; QU = Quarantined; TF = Transfused; DS = Destroyed; SHIP = Shipped

SOP # attachment #
Effective date

Figure 11–1 Sample lookback worksheet.

Date: December 1, 2005

John Doe, MD
Director, Blood Bank
General Hospital
Anywhere, CA 90000

This confirms our telephone notification that your hospital received a blood component from a donor that was subsequently found to be confirmed positive for HIV-1. All test results from prior donations were nonreactive, including those for the blood component shipped to your facility.

On November 30, 2005, at 11:25am, we telephoned your facility and spoke to Jane Doe and conveyed the following information:

UNIT NUMBER	Z987654321
TYPE OF COMPONENT	Whole Blood
ABO/RH:	O negative
EXPIRATION DATE:	12/6/2005
SHIPMENT DATE	11/25/2005

Your transfusion service reported the unit to be **transfused.**

Please complete and return the enclosed *Lookback Product Disposition Record*. Maintain a copy of the record for your files.

If you have any questions concerning this matter, please contact the Somewhere Donor Center at (555) 123-4567 x891.

Sincerely,

Name & credentials
Authorized Somewhere Donor Center contact

Figure 11–2 Sample confirmation letter.

on a facility's own initiative, by FDA request, or by FDA order under statutory authority. FDA guidelines categorize all recalls into one of three classes according to the level of hazard involved.

A Class I recall is a situation in which there is a reasonable probability that the use of or exposure to a violative product will cause serious adverse health consequences or death. An example of products in this category would be a unit issued that was found to be HIV positive.

A Class II recall is a situation in which use of or exposure to a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote. An example of products in this category would be a unit later found to be collected from a donor whose hemoglobin did not meet the minimum criteria.

A Class III recall is a situation in which use of or exposure to a violative product is not likely to cause adverse health consequences. Examples of products in this category might be those that do not meet FDA labeling regulations.

Somewhere Donor Center
123 Main Street
Anywhere, State, Zip
(555) 123-4567 extension 891

Section A: *To be completed by Somewhere Donor Center*

Case ID: _____

Consignee: _____ Contact Person: _____

Street Address: _____ Phone: _____

City/State/Zip: _____ Email: _____

Re: (Unit number) _____ ABO/Rh: _____ Component: _____

Date Shipped: _____ Expiration Date: _____ Date Notified: _____

Reason for Notification: _____

Form Completed by: _____ Date: _____

Section B: *To be completed by Consignee*

Final Disposition of Component: _____ Date of final disposition: _____

❑ Transfused
❑ Returned
❑ Discarded (Reason) _____

❑ Transferred to another facility (Please complete the information on the receiving facility below)

Name _____
Street Address _____
City/State/Zip _____
Phone ( ) _____

Informed ❑ No ❑ Yes If Yes, Date notified _____

For Manufacturers only: ❑ Put into production ❑ Quarantined ❑ Discarded

Form Completed by: _____ Date _____
Title _____

Figure 11–3 Sample lookback product disposition record.

A market withdrawal occurs when a product has a minor violation that would not be subject to FDA legal action. The firm removes the product from the market or corrects the violation. For example, a product removed from the market due to tampering, without evidence of manufacturing or distribution problems, would be a market withdrawal.

Biological Product Deviation Reporting

On November 7, 2000, the FDA published a final rule[160] to amend the requirements of reporting errors and accidents in manufacturing of products. This rule was issued as part of a program to improve the effectiveness of the FDA's regulatory program. FDA replaced the term *error and accident* with the term *biological product deviation* (BPD).

Licensed blood establishments, unlicensed blood establishments, registered blood establishments, and transfusion services are required to report to the FDA all BPDs. BPDs are defined as any event associated with manufacturing of blood or blood components that EITHER:

1. Represent a deviation from current GMPs, applicable regulations, or established specifications that may

affect the safety, purity, or potency of that product OR

2. Represent an unexpected or unforeseeable event that may affect the safety, purity, or potency of that product AND
   - Occurs in your facility or a facility under contract to you AND
   - Involves a distributed blood or blood component.

Post-donation information is considered reportable to the FDA as a BPD if the donor should have been deferred had the information been known at the time of donation and the safety, purity, or potency of the product could be affected. Post-donation information also includes information that a blood center obtains when it adds new donor history questions.

In many cases blood establishments cannot control post-donation information. For example, a donor may call after donating to report a post-donation illness, or information obtained post-donation about exposure to a disease or a sex partner at high risk. Reports of post-donation information continue to represent the largest percentage of BPDs submitted by blood and plasma establishments (71%). In 88% of the reports the donor was aware of the information at the time they were interviewed, but failed to provide the information during the interview. Most often (91%), the donor center staff is made aware during a subsequent donation interview.[161]

CONCLUSION

The products of blood donation—RBCs, platelets, and plasma—are a vital resource making possible modern medicine. At this time, there are no comparable substitutes. A debt of gratitude is owed to those blood donors who give their blood, for no monetary compensation, to anonymously help save the lives of others.

At one time, all that was needed to collect blood was a collection set and a donor with suitable veins. Since then, thousands of transfusion medicine professionals have transformed the early donor rooms to a multibillion dollar industry collecting tens of millions of blood products per year. Their ceaseless efforts to improve transfusion safety have had remarkable success on the well-being of the blood recipient, donor, and even the collections staff. Unremitting efforts to improve donor screening and serologic testing for infectious disease are needed to keep ahead of potential threats to the blood supply.

For these reasons, change occurs very rapidly in the world of blood banking, and all decision-making processes require checking for the latest information available, which can be obtained through the AABB or FDA websites.

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