CHAPTER 4

Recruitment and screening of donors and the collection, processing, and testing of blood

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The blood donation and transfusion chain

Although much effort has been expended to find suitable replacements for blood components, the best source continues to be blood collected from healthy, human donors. The process of supplying sufficient blood components and derivatives for patient needs is complex and highly regulated. At the same time, it must be dynamic in adapting to the local and regional needs for providing blood products that may have a short shelf life. Other chapters have detailed descriptions of how to prepare and preserve red blood cells (RBCs; Chapter 9), platelets (Chapter 19), granulocytes (Chapter 23), and plasma and plasma derivatives (Chapter 27). This chapter focuses on the donation and collection process, from recruitment of donors to the receipt of products in the hospital inventory. Physician involvement is essential to this process.1

An overview of the entire blood donation and transfusion chain is seen in Figure 4.1.2

The role of hemovigilance as the last step of the chain has become increasingly emphasized over the past decade (see Chapter 6). Hemovigilance is “a set of surveillance procedures covering the whole transfusion chain from the collection of blood and its components to the follow-up of its recipients, intended to collect and assess information on unexpected or undesirable effects resulting from the therapeutic use of labile blood products, and to prevent their occurrence and recurrence.”3 The entire process is typically under intense regulatory scrutiny from governmental agencies and industry groups such as AABB (formerly known as the American Association of Blood Banks, see www.aabb.org) and the Plasma Protein Therapeutics Association (www.pptaglobal.org). Details on the regulatory aspects are addressed in Chapter 7. In many countries, there are dual systems for supplying blood for patient transfusion in the hospital, and for collecting source plasma for derivatives. This is due to parallel development of these systems during the latter half of the 20th century. This is reflected in the arrangement of this chapter, with separate sections for collection of transfusable products and source plasma.

In this chapter, an introduction to the organization of blood services responsible for managing this complex process will be covered first. Recruitment of blood donors will then be described, followed by a detailed analysis of the donation process from the perspective of the donor and also of the component prepared. Finally, source plasma donation will be addressed. Donor adverse events are considered in Chapter 5.

Organization of blood services to meet global needs

In 2012, 108 million units of blood were collected worldwide.4 The use of blood is very heterogeneous among countries. For instance, in low-income countries, two-thirds of transfusions are given to children under 5 years of age; whereas in high-income countries, three-fourths of all transfusions are given to patients over 65.4 In high-income countries, blood is most commonly used for supportive care in cardiovascular surgery, transplant surgery, massive trauma, and cancer therapy. In other countries, it is used more often to manage complications of pregnancy and severe anemia in children.5

Various successful models have been developed to deliver blood products. The worldwide spectrum of blood service organization is diverse, and it varies based on local health initiatives, government intervention, historical development, and available resources. In this section, a brief history of blood collection services will be addressed first, followed by a discussion about the organization of blood services in the United States and then an introduction to blood services outside of the United States. A more extensive history of transfusion medicine is detailed in Chapter 1.

The British Red Cross is credited with establishing the first organized blood donor service in 1921, identifying a panel of potential donors who would provide fresh blood at the time it was needed.5 In 1935, the International Society of Blood Transfusion (ISBT) was established as a scientific and educational society to bring together professionals involved in blood transfusion and transfusion medicine worldwide (www.isbt-web.org). By 1935, a number of blood centers had been established in Russia, at least two of which were providing blood for patient care.6 Cook County Hospital in Chicago became the first blood bank in the Western world to store blood for future use in 1937.5 The first community blood center was established in 1941 in San Francisco, California. Significant advances in transfusion medicine occurred over the next decade, when the National Blood Service was established in the United Kingdom (1946) and the American Red...
Cross began its National Blood Program for civilians (1948). World War II provided a great stimulus for the development of blood donor services. The extraordinary efforts of a number of individuals in different countries to provide this lifesaving resource have been documented elsewhere.7

**Organization of blood services in the United States**

Blood collection for transfusion in the United States is accomplished by an eclectic system that has evolved since World War II. Close to half of the blood for transfusion in the United States has historically been collected by the American Red Cross (www.redcross.org). Community blood centers were established nationwide in areas where the Red Cross did not operate. Most of these nonprofit collection agencies are now loosely affiliated with a trade organization known as America’s Blood Centers. Members range from very large blood programs such as Blood Systems (founded in 1943—see www.unitedbloodservices.org), New York Blood Center, and OneBlood (Florida based), to very small one-county programs. In addition to community blood centers, a number of hospitals also started collecting blood for their own use.

The concept of regionalization of blood services emerged from the assumption that a blood center should serve the surrounding areas that referred patients to major city medical centers. This allows the entire geographic area to support the needs of its patients, whether they are cared for in the community or a referral center. By managing the blood within a region in a systematic way, waste can be reduced through the use of technological innovations and careful inventory management. There are resource-sharing arrangements that allow organizations to move blood around to different centers that are in need of blood.

In response to the transfusion-transmitted acquired immune deficiency syndrome (AIDS) epidemic of the 1980s, the US Food and Drug Administration (FDA) increased blood industry accountability to levels similar to that of pharmaceutical regulation (see Chapter 7). Blood centers found themselves implementing quality assurance programs with dedicated personnel to assure compliance within the new regulatory framework. The voluntary AABB accreditation program likewise moved from an inspection and accreditation focus to one on quality systems. As organizations struggled to conform to this new paradigm, a number of blood centers were placed under judicial consent decree for failing to meet regulations—including three of the largest collection organizations in the United States. A significant portion of the blood used in the United States today is provided by

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**Figure 4.1** The blood donation and transfusion chain: from donor arm to patient vein. The bold arrows outline nine important stages in the system that assures safe and effective patient blood transfusions. Graphic design by Kimberly E. Crookston. Source: Crookston et al. (2015). Reproduced with permission of Lippincott, Williams & Wilkins.
organizations that still remain under court supervision due to judicial consent.

Competition for market share was not well received by many of the nonprofit monopolies that felt blood was more of a gift than a commodity. These centers viewed their mission primarily as community service, linking donors with recipients. This view of blood as a commodity did not diminish as mergers, acquisitions, and consolidations affected blood collection agencies in parallel with the changing healthcare industry. By the end of the 20th century, competition had lessened and the relationship of blood centers with hospitals began shifting from a commodity-based relationship to one valuing service, medical expertise, and patient outcomes. However, it was soon realized that healthcare expenses were rising more quickly than other parts of the economy, particularly in the United States. Through aggressive reorganization and cost control strategies, the price of blood has decreased. This has been accompanied by a decrease in demand for RBCs (see Figure 4.2). The annual blood transfusion rate in the United States (RBCs/whole blood) decreased from 54 allogeneic units per 1000 people in 2004, to 49 in 2008, and to 44 in 2011. The donation rate per unit population of 76.2 was the lowest reported since 1997. Although these trends correlate with the global financial crisis of 2008 and the growth of patient blood management programs, the specific cause of the decline is not fully understood. Patient blood management is discussed in Chapter 2. In brief, it is a multidisciplinary approach to improve patient outcomes using evidence-based strategies in patients who may need transfusion. The goal is to improve outcomes, not only by transfusing blood appropriately but also by introducing strategies to prevent patients from needing a transfusion in the first place.

Many blood centers are affiliated with national blood banking organizations, including AABB (founded in 1947—see www.aabb.org). The “voluntary” standards set by the AABB are so well regarded that these often become the standard of care in North America and in other areas of the world, even without government regulatory intervention.

Many hospitals have found it impractical to maintain hospital-based collections. Although hospital-based collection still exists in the United States, the increasing cost, external regulation, shortage of medical technologists, and variable supply and demand have progressively shifted collection activities to blood centers. However, the proportion of blood collected by hospitals in 2011 remained relatively constant when compared to 2004 (6.6 vs 6.4%, respectively). Even hospitals that collect their own blood usually do not perform donor testing, and out of necessity they maintain a supplemental blood contract with the local blood supplier. The US Department of Defense continues to operate an independent blood services organization for its hospitals as well as its military mission.

Blood components collected for transfusion in the United States are from volunteer donors; in contrast, most plasma for fractionation is collected from paid donors, as discussed later in this chapter.

**Organization of blood services outside the United States**

Most high-income countries have adequate blood services, maintaining a full range of donor screening and quality assurance procedures, while producing most of the components needed in the region. However, there exists a wide variety of dissimilar organizational structures that are successful in meeting the transfusion needs of areas served. These models can be centralized or decentralized, governmental, military, private, hospital based, or mixed. For the most part, the local transfusion system reflects the administrative system of each country. For instance, in countries that have strong governmental control, there is often a centralized transfusion system operated by government-run institutions. The World Health Organization (WHO) encourages strong governmental leadership in establishing national transfusion networks. Many countries outside the United States have instituted national blood programs. Overall, the provision of blood services worldwide is heterogeneous and varies with historical development, the socioeconomic development of the region, and the influence of national scientific and political factors.

Donor recruitment is sometimes performed externally to the blood collection agencies. Recruitment is sometimes carried out by independent organizations that have a special relationship with the procurement agency, such as a country’s national Red Cross. The International Federation of Blood Donor Organizations was established in 1955 as a support network for donor recruitment (www.fiods-ifbdo.org). Seventy-two nations participate, although there is a notable absence of many English-speaking countries. The goal of the organization is member state self-sufficiency in blood from voluntary, unpaid blood donors, while also improving safety and, in turn, confidence in the national blood supplies by developing minimum standards for donations, inspection, and quality assurance.

In 1975, the 28th World Health Assembly passed a resolution recognizing the value of voluntary blood donation and called on member states to promote national blood transfusion services based on voluntary unpaid donations. Voluntary donation has been a goal for some time, as it is perceived as a safer alternative. In 2002,
the European Union approved legislation that established comprehensive standards for blood products that included a requirement for voluntary donation. The WHO Global Database on Blood Safety 2011 report presents data from 164 countries representing 92% of the global population. It shows that half of the global blood collection occurs in high-income countries, home to only 15% of the world population. Global blood donations from voluntary unpaid donors increased from 2004 to 2012. Seventy-three countries collect over 90% of their blood supply from voluntary unpaid blood donors. However, 72 countries collect more than 50% of their blood supply from family/replacement or paid donors. Around 1.5 million donations intended for transfusion were collected from paid donors. Nevertheless, countries are increasingly moving toward voluntary blood donation.

WHO recommends that, at minimum, all blood for transfusion should be screened for HIV, hepatitis B, hepatitis C, and syphilis. Twenty-five countries are not able to screen all donated blood for one or more of these infections. Irregular supply of test kits is one of the most commonly reported barriers to screening. Yet, even in countries that are able to screen all of their blood, the risk of transfusion-transmitted infections (TTIs) varies. The prevalence of TTIs in blood donations in high-income countries is considerably lower than in low- and middle-income countries. External quality control assessment is often lacking; whereas 97% of blood-screening laboratories in high-income countries are monitored, only 33% of middle-income and 16% of low-income countries have external quality assessment.

There is still heterogeneity in the practices that are taken for granted as mandatory in North America, even among the most effective blood services. For instance, in Norway, nucleic acid testing for HIV is not performed on repeat blood donors due to the low incidence in the recruited donor population and the effectiveness of the serological screening.

Low- and middle-income countries often struggle to provide the same level of safety as high-income countries with established blood procurement systems. The costs of procurement and testing of the blood are often prohibitive. For instance, in sub-Saharan Africa, although blood transfusion has a long history, collection services are fragmented. Blood is sometimes in short supply, and safety seldom can be guaranteed.

Some high-income countries such as the United States have implemented a “precautionary principle” that has meant extreme costs for marginal added safety when measured by standards such as quality-adjusted life-years. Many countries simply do not have resources to implement this strategy, even if it were medically justified. In stark contrast to the precautionary principle, blood in some parts of the world is still transfused without testing. In addition, when testing can be done, there may not be resources to notify and counsel donors about positive test results, such as HIV. This provides an opportunity for the world community to make a great impact on global health through collaboration and collegiality. In response, WHO established the Global Collaboration for Blood Safety in 1994, a voluntary partnership of organizations, institutions, associations, agencies, and experts that are concerned with the safety and availability of blood. Many of these functions are now carried out by the WHO Global Blood Safety Network and the WHO Global Forum for Blood Safety (http://www.who.int/bloodsafety/collaboration/en/).

**Recruitment of blood donors**

The first task of a regional blood center is to recruit adequate numbers of donors to provide for patient needs. Traditionally, this requires a strong association between the blood center and the population in an area, as well as the cultivation of an altruistic spirit and a sense of social responsibility within the community. As described by Titmuss, the act of giving blood clearly demonstrates the integration of individuals into society. However, there exists a fragile balance between blood supply and blood demand in the United States. Previous calculations estimated this number at 177 million eligible blood donors. These findings come at the same time that the baby boomers, a mainstay of the donor base, approach those years when exclusionary factors increase and only a small fraction of eligible donors donate the “gift of life.” The recruitment of blood donors is now the most challenging task at the blood center. Blood donation is one of few “gifts” that involves physical insult to the body, conceivably offering a higher level of service than giving of one’s time or money. The gift of blood is most often given to an unknown individual with no direct thanks or appreciation or knowledge of the transfusion outcome. The thanks and appreciation must come from the blood center, the steward of the community’s blood supply. Data from the following discussion of donor recruitment have been derived mainly from the volunteer donor populations in the United States and Canada. The blood donation rate in high-income countries such as these is 36.8 donations per 1000 population. The rates in middle- and low-income countries are 11.7 and 3.9 donations, respectively.

Many studies have attempted to explain why people do, or do not, become blood donors.

Other studies have sought to determine the motivation to repeat the donation process. These studies have evaluated demographic and sociological/psychological characteristics as well as donor motivation for giving or not giving blood. The challenge is to use these findings and apply them to the everyday recruitment of blood donors.

**Donor demographics**

The demographics of current blood donors provide the blood center with insights into where and to whom they might focus marketing and recruiting efforts. As expected, individuals who are integrated into American society at upper socioeconomic ranges are more likely to volunteer in community efforts, give money to charitable causes, and donate blood than individuals in marginalized populations who are struggling at lower socioeconomic levels. Donors who are older (>50 years) and who have more education (college graduates) are more likely to return as repeat donors than those who are younger and who have not gone to college. Other studies have observed differences in donation rates among minority groups that exist apart from socioeconomic status. Thus, as the population at large continues to become more diverse, blood donor organizations are ever more challenged to recruit a more widely representative group of donors who are not reflected in the traditional donor pool.

Current donors in the United States included a significantly higher proportion of females aged 45 or older, white, college graduates, repeat donors, persons married or living as married, and born in the United States. When comparing the demographics of a group of donors who had donated five gallons or more with a group of randomly selected donors, the five-gallon-or-more donors tended to be white, male, college graduates, and regular voters with an average age of 52. First-time donor demographics at five US blood centers between 1991 and 1996 noted a continuing high proportion of first-time donors younger than 35 years of age who were white non-Hispanic and US-born with a college degree or
higher. There was, however, a significant increase in the proportion of non-US-born first-time donors at each blood center over the six-year period with a concurrent decrease in the proportion of white donors.  

Return behaviors of blood donors in comparison to donor demographics have also been evaluated. In general, younger donors were the least likely to return. With increases in age, return rates increased to over 40% for those aged 50 and older. Multiple-return rates were highest among college graduates and lowest among donors with no more than a high school education. In evaluating older volunteer blood donors with a mean age of 68 years, the majority was married, well educated, and somewhat affluent. Additionally, when returning first-time donors were compared with nonreturning donors, returning donors were more likely US born, white, better educated, and older.

Donor motivation
Studies continue to show that the concept of altruism has been associated most often as the reason for giving blood. In volunteer blood programs across the globe, the unselﬁsh act of giving blood for the welfare of others remains the centerpiece of blood donor recruitment initiatives. But other motivators include the concepts of community need, and social pressure to conform to expectations or desires of an individual or group. People may donate because someone asked them to, they have heard about an emergent need for blood, or others are doing it. Convenience to donate has also been identiﬁed as an important factor, and blood centers understand the value of strategically located ﬁxed donation sites and the need for mobile operations.  

More recent studies have examined the role that incentives have on donor motivation. Blood credits (e.g., credit toward blood units required by members of a family or community group) were most attractive to donors as incentives, as well as cholesterol screening and a prostate-speciﬁc antigen (PSA) screen in men. In general, small incentives or tokens of appreciation were more likely to appeal to younger donors than older donors. In a follow-up study, ﬁrst-time donors were positively inﬂuenced with incentives, but this ﬁnding was also related to the younger age of these donors. In another study, ﬁrst-time donors were more likely than repeat donors to be encouraged to donate and less likely to be discouraged if offered cash, event or lottery tickets, or merchandise. Donors attracted by cash were more likely to have a risk for TTIs. Medical testing and blood credits were attractive to both ﬁrst-time and repeat donors.  

Nonetheless, blood shortages have continued to raise the question of compensation for donation. The concept of targeted and selective nonmonetary incentives for certain populations, such as lapsed donors during times of shortages, continues to be raised.

Younger and ﬁrst-time donors also decided to donate because of a family member, friend, or coworker. Younger and ﬁrst-time donors were also motivated to donate because of testing for infections. When compared to donors with a high school education or less, donors with a college or higher degree were more likely to donate because it was the right thing to do, and less likely to donate to improve their health (e.g., by receiving a PSA or cholesterol screening) or because of family or peer inﬂuence. Men tended to donate more often than women because it is good for their health, they wanted to be tested, or they wished to receive an item or gift. Women tended to donate because it was the right thing to do or because they had heard about a need for more blood. More than 90% of respondents to a questionnaire administered to Asian, black, Hispanic, and white donors cited a desire, responsibility, or perceived duty to help others as an important or very important motivator to donation. Being asked to participate in a work-related blood drive was also an important motivator, and not being asked was a deterrent. Getting the results of a health screen appealed to many and was most important to black and Hispanic donors. More than 50% of respondents did not ﬁnd any of the incentives (gifts, tickets, time off work, or reward) important at all in their decision to donate.  

In a 2005 Canadian study, the importance of altruism as a motivator to donation was noted along with family and social inﬂuences. Blood centers need to identify potential donors who are more likely to be motivated by the message to "make it available for themselves if required" versus a message to "make it available for someone close to you." In another randomized controlled trial, donors received information about the indication for transfusion of their blood and the recipient’s status. Donors were enthusiastic about receiving this information. However, as the study was performed in a highly committed blood type O-negative donor population, no signiﬁcant increase in donation frequency could be demonstrated.

Deterrents to donation
There are many deterrents to blood donation. Some deterrents, such as inconvenience, perceived incompetence of personnel performing blood collection activities, and the lack of cleanliness of a given facility or operation, are clearly within the control of the blood center. But some deterrents, including the perception that blood donation is not important, the belief that one can contract a disease by donating, and the desire to remain ignorant of any positive results from infectious disease testing on the donation, are more difﬁcult to overcome.

The most frequently mentioned negative motivator to donation is fear, including fear of needles, seeing blood, weakness, dizziness, and discomfort. In some individuals, these types of fears may never be overcome. Education programs tailored to overcome fear and heighten the awareness of need may be helpful. Medical disqualiﬁcation is also a frequently given reason for nondonation. However, several studies have shown that many perceived reasons for nondonation have been invalid or imagined. At least for some individuals, invoking a medical disqualiﬁcation is more appealing than admitting to some type of “fear” relative to blood donation.

Treatment by blood center staﬀ and the donor’s perception of staﬀ competence, coupled with donor sense of well-being during and after donation, inﬂuence the likelihood of donor return, although highly committed donors are generally not deterred by the occasional bad experience during donation. Blood donation–related symptoms including dizziness, nausea, and fainting are a signiﬁcant reason for donor nonreturn. Several strategies have been proposed to mitigate symptoms and increase donor returns.

Temporary deferral has a signiﬁcant impact; deferred donors return less frequently than nondeferred donors and are more likely to lapse from donation. In a further study, repeat donors who reported a previous temporary deferral were more likely to lapse, but the association disappeared when other factors such as accessibility, satisfaction with last donation, and perceived need for blood were adjusted. Of interest, several lapsed donors incorrectly viewed themselves as permanently deferred for temporary conditions such as low hemoglobin or hematocrit.
Sociological and psychological theories of blood donation

Many theories exist about donor motivation, and several excellent reviews are available with more detail on this complex aspect of blood donor recruitment.58–53 Opponent-process theory has been used to explain why some individuals repeat the process of donation and become committed, habitual blood donors. Donors experience a “warm glow” after donation, which may represent an opponent process in response to negative feelings experienced before and during initial donations.

Attribution theory suggests that people who have taken an action (e.g., donating blood) without external coercion or large reward are likely to attribute to themselves a predisposition toward that action. Once they have attributed such a tendency to themselves, or once they decide that they are “the kind of people who do such things,” they are more likely to act in ways consistent with that attribution in the future.

In the model of commitment, four processes are proposed: coping with and neutralizing the negative aspects of donation; developing internalized motives for donation and integrating them into one’s self-concept; developing a behavioral intention to continue giving blood; and, finally, developing a self-sustaining habit of donation.

The theory of reasoned action states that all behavior is preceded by a behavioral intention that can be measured by seeking an estimate of the probability of acting on that specific behavior. Intention is a function of two additional factors: the individual’s attitude toward performing the act, and the perceived expectations of others for what one should do in a particular situation. This theory has been, in general, effective in explaining donor action related to blood donation. For example, donors who verbally expressed their intention to donate when recruited were more likely to attend the drive than those who were merely reminded. Once they have attributed such a tendency to themselves, or once they decide that they are “the kind of people who do such things,” they are more likely to act in ways consistent with that attribution in the future.

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The attitudes of donors and nondonors in three areas including affect, cognition, and behavior have been reported.34 In terms of affect, donors were more likely to indicate that blood donation made them feel generous, assured, relaxed, and useful. Nondonors were more likely to indicate that donation made them feel uncomfortable and ill. On cognition scores, more nondonors believed that blood donation was dangerous and appeared to know little about the process. Donors were more likely to cite that blood donation is worth any inconvenience and is an important civic duty. For behaviors, donors ranked more favorably those behaviors that reflected the donation process. The authors concluded that blood donor behaviors may be more strongly determined by affective and emotional processes rather than by carefully reasoned decisions.34

It appears from the literature that the model most likely to predict future blood donation behavior is the theory of planned behavior.55,56 This model postulates that behavior can be determined by intentionality, which in turn is affected by attitude (positive or negative evaluation of the behavior), subjective norm (perception of social pressure), and perceived behavioral control (perceived ease or difficulty in performing the behavior). Several studies involving nondonors concluded that this model predicted 31–72% of the variance in intention to future blood donation. In a study based on the theory of planned behavior and experienced donors, 65% of the variance in donation intention and 50% of the variance in attitude were accounted for.56 Self-efficacy showed the strongest positive relationship to donation intention, followed by attitude, subjective norm, satisfaction, and personal moral norm. Prior vasovagal reactions related negatively to intention to donation.57

Once a recruited donor presents to donate at a blood or plasma center, a highly regulated process ensues. This process will first be outlined for volunteer donors, followed by a separate section for plasma donors.

The collection process for blood components for transfusion: screening, phlebotomy, choice of product, collection, testing, and distribution of blood and apheresis components

Donor evaluation

The twofold purpose of blood donor screening is to minimize the risks to both the blood recipient and the donor (see Figure 4.1 and Chapter 5). Donors should be informed as early as possible about all aspects of the donation procedure and about the importance of critical self-evaluation and self-exclusion for those who do not qualify. Pre-recruitment information about donor qualifications and pre-donation information about risk factors for transmitting infections through transfusion should lead to self-deferral by some donors. When the donor presents for donation, written educational material is given, including a list of deferral medications.

Answers to donor history questions in a confidential setting provide another opportunity to obtain information about potential risk. Only three years after the founding of AABB, a list of 21 diseases and conditions were introduced on the “donor record card” that was intended to be used nationwide for screening criteria.58 This was based more on the medical judgment of the day than on clear-cut data or evidence. Many of the current medical deferrals are still based less on data and more on a combination of opinion, tradition, and “conventional wisdom.”58 With the advent of HIV, a second phase in the development of the questionnaire was based on epidemiologic evidence and included direct questions about sexual risks. The FDA stressed a face-to-face interview, rather than filling out a questionnaire, in hopes of ensuring complete honesty in answering the questions. Such data as history of hepatitis and possible exposure to HIV are used to deter donations from persons with potentially infectious exposures. This is done in order to reduce the pretest probability of finding true-positive results during laboratory testing. In other words, the precollection donor-screening process reduces the amount of blood collected that can transmit infectious diseases. Although laboratory testing is very sophisticated, it can never completely eliminate the risk of an infected unit. Reducing the number of infectious units that make it to the testing laboratory will reduce the number of infectious units that make it through the testing process undetected (i.e., false-negative test results).

The donor questionnaire is a dynamic document that is updated as new risks become apparent.34,35 The interview process will be ineffective if it becomes too onerous or lengthy. If there are too many questions, important issues about high-risk behavior might be obscured, and the ultimate purpose of the interview process
would be defeated. In the United States, an effort has gone toward creating a Uniform Donor History Questionnaire (UDHQ) to standardize criteria used for all tissue and blood donations and reduce the complexity, burden, and possible confusion. Donors are queried using broad-based capture questions to make screening more efficient. Certain questions are designed to eliminate the need for further exploration of the subject if the answer is no. The questions are asked reverse chronologically. Questions start with the day of presentation, proceeding backward, and query about donor health status, travel, medications, and other items associated with increased risk to either donor or recipient (e.g., “In the past 48 hours . . .,” “In the past 6 weeks . . .,” “In the past 12 months . . .,” or “Have you ever . . .”). Some medications are deferring because the indication for use increases the donor’s risk in donating (e.g., antiseizure medications), and others are deferring in order to protect blood recipients (e.g., the use of potentially teratogenic medications such as isotretinoin). Still other medications might suggest a condition where the donor may not be able to give informed consent (e.g., Alzheimer’s disease).

A comprehensive treatment of the screening process has been published.59 Questions deal with items such as the following:

- Current state of health;
- Medication use (including aspirin);
- Pregnancy;
- Recent blood donations or immunizations;
- Receipt of a transfusion, transplant, or graft;
- Sexual practices that may increase the risk of HIV;
- Body piercing or tattoos;
- Incarceration;
- Exposure to hepatitis;
- Travel to areas where certain diseases are endemic (e.g., malaria, variant Creutzfeldt–Jakob disease, and Chagas disease);
- Use of clotting factor concentrates;
- Injection of any drugs not prescribed by a physician; and
- History of diseases such as malaria, Chagas disease, babesiosis, cancer, cardiovascular disease, a bleeding condition, or a family history of Creutzfeldt–Jakob disease.

The most recent questionnaire and accompanying educational materials may be found online by following this path on the AABB website: http://www.aabb.org > Give Blood > Donor History Questionnaires > Blood Donor History Questionnaire. An abbreviated questionnaire has been developed for recent repeat donors that eliminates nonrepeatable events from the questionnaire.63 Most US blood centers have adopted the UDHQ.

During the interview, prospective donors might become aware of disqualifying factors in the health histories but feel too embarrassed or coerced to admit to disqualifications. Provisions must be made at all collection sites for persons to exit at any time without examination, and the opportunity must be provided for the donor to easily indicate that collected blood not be used for transfusion. Mechanisms have been established for confidential unit exclusion that provide for this, either at the donation site using a confidential form or barcode, or by anonymous telephone call after donation.

Donors also receive an abbreviated physical examination, including monitoring for symptoms of current disease processes, body temperature, heart rate and rhythm, and the ability to comprehend the screening questions and give informed consent. Informed consent for donation should also include the possibility that the donor will be listed in a deferral registry if the history or testing precludes donation. In some areas, laws may require that public health authorities be notified when donors test positive for certain diseases.

A blood sample is tested before donation to make sure the hemoglobin is at least 12.5 g/dL using an instrument, or a spun hematocrit ≥38%, to screen for anemia (recently increased to 13.0 g and 39% for male donors). This is the minimum requirement for allogeneic whole blood donation in the United States and many countries. Other automated procedures such as red cell, platelet, and plasma collection byapheresis technology may require more rigorous hemoglobin cutoffs and have minimum height and weight guidelines. Blood centers in the past most often measured red cell mass using copper sulfate, but recently more objective measurement methods that measure hemoglobin or hematocrit have been employed. In the copper sulfate method, a drop of capillary blood from a fingerstick sample is dropped into a copper sulfate solution with a specific gravity of 1.053. Sinking of the drop indicates a hemoglobin of 12.5 g or above. The copper sulfate method, although well accepted for decades, suffers from problems with both specificity and sensitivity. Because of the former, donors who fail are often retested with a spun hematocrit. This test can also err in accepting individuals who are proven anemic by a venous sample taken at the same time.60,61

A prospective donor with a diagnosis of chronic, degenerative, or infectious disease should be deferred from blood donation. Donors whose histories carry significant risk and those who have tested positive for infectious diseases are placed on deferral registries. For some deferrals, “reentry” pathways back into the donor pool have been made available when the risk is no longer present. On occasion, donors attempt to donate in spite of permanent deferral. Reasons include a desire to obtain results of infectious disease testing, to receive credit for community service, a misunderstanding about the reason for deferral, and erroneous recruitment by the blood center staff.62

The effectiveness of the donor interview in deferring individuals who have risk factors that could impact the safety of the product has been a subject of investigation. The Retrovirus Epidemiology Donor Study has shown areas where improvement is needed. Younger donors (less than 25 years of age) have a higher behavioral risk factor than older donors. Educational reinforcement is needed for this group.63 Most donors skim the educational material and fail to assimilate the information. Thus, more effective materials are needed. However, some high-risk donors seem resistant to any attempt at education, and test-seeking behavior is a particular problem.64-66

Computer-assisted self-interviewing (typically using a touch screen) has become an increasingly popular vehicle for donor screening. Data from this group suggest that it is probably able to reduce the number of high-risk donors by increasing self-deferral.67

Acceptable donor age is 17 and above in most centers, but there is considerable variation in practice. Recent efforts have convinced some governments to allow 16 year olds to donate. Experience with healthy donors over the age of 65 has generally been favorable; thus, the need for an upper age limit is questionable.29

In 2011, 18.0 million individuals presented to donate in the United States, 93.5% of whom were at blood centers; 31% were first-time donors, and 2.46 million of these donors were deferred (13.7%, an increase from 12.6% in 2008). Of these, 48.8% were deferred for low hemoglobin and 1.4% for high-risk behaviors; 1.1% of successful donors had the units destroyed due to abnormal disease markers.11 Once the donor has been appropriately evaluated to insure that the risk to the donor and to the recipient is acceptable, then blood collection may occur.
Blood collection

This section will first address the traditional collection of whole blood and its separation into components, followed by discussion of newer automated apheresis technology.

Whole blood collection

Despite the many technologies for automated collection, some blood centers—indeed, entire countries—are able to produce the bulk of needed inventory from whole blood collections. A typical whole blood collection takes 45–60 minutes, including the interview, physical exam screening, aseptic scrub, antecubital vein venipuncture, and monitoring for postdonation reactions in a canteen area where refreshments are offered. The blood draw itself should be accomplished in approximately 10 minutes, with periodic agitation to mix the fresh blood with the anticoagulant in the draw bag to reduce clotting. The tubing is clamped before the needle is removed so that air is not drawn into the blood bag. Blood samples are taken into pilot tubes for testing. This is normally done from the blood tubing at the conclusion of the donation or from a diversion pouch filled from the first blood collected, a process that captures contaminating skin organisms. The tubing is sealed, and the needle is discarded without recapping. The donor holds firm pressure over the venipuncture site, and then a pressure bandage is applied. The donor is instructed to keep the pressure bandage on and avoid strenuous activity for a prescribed amount of time, to increase fluid intake for the next day or two, and to spend at least 15 minutes in the canteen area. Reactions usually occur at the end of donation in the donor chair or in the area where refreshments are served. If the donor leaves immediately against advice, risk of injury might be increased. Staff monitoring the postdonation canteen area must be vigilant in assessing for signs of reactions and proactive in preventing fall injuries.

Whole blood collection has the longest cumulative experience and requires fewer resources than automated collection. For countries in the process of developing simple, reliable collection networks, whole blood is the logical first step, with or without component separation.

Component separation

Whole blood may generally be stored for up to 21 days. Whole blood may be separated by centrifugation into RBC, platelet, and plasma components according to density. This allows longer shelf life, better inventory management, and more choices and resources for patient care. The capacity to provide patients with the different blood components they require is still limited in low-income countries: 45% of the blood collected in low-income countries is separated into components, 80% in middle-income countries, and 95% in high-income countries.

Using a “closed” separation system that is not ever open to outside air is important to prevent contamination with microorganisms during collection and component separation. Centrifuge-separated components are transferred from the original whole blood draw container to satellite bags through integrally connected plastic tubing. Adding nutrients and saline to the RBCs permits storage at 1–6 °C for up to 42 days (see Chapter 9). The preservative solution may be held sterilely in one of the integral transfer bags until the plasma is separated off into a third bag after centrifugation. Then the solution may be added back to the packed RBCs in the original bag.

Platelets may be separated from the whole blood or allowed to degenerate without being separated. In Europe and many areas of the world outside the United States, “buffy-coat” platelets are produced by using a “hard” spin initially to separate all cellular elements from the plasma. Then theuffy coat containing the platelets, white blood cells, and a significant contaminant of RBC is further processed to isolate the platelets. In the United States, an initial “soft” spin separates platelet-rich plasma from the RBCs, and then a “hard” spin separates the platelets from the plasma. Additional information about platelet preparation and storage may be found in Chapter 19. Platelets are typically stored for 5 days at controlled room temperature before expiration. In 2011, 3.9 million platelet apheresis/pools were transfused in the United States—a decrease of 13.4% from 2008.11 The ratio of doses of apheresis platelets to whole blood–derived platelets rose from 7:1 to 10:1 during the same period. About 12.8% of platelets produced in 2011 expired, due to the short half-life and logistical challenges.11

Platelet separated and frozen within 8 hours is called fresh frozen plasma (FFP), whereas that frozen up to 24 hours is known as FP24. Each contains coagulation factors in quantities adequate for most patient indications. FP24 represented only 15% of the 4.1 million units of plasma transfused in the United States in 2004 but 47% of the 5.9 million units of plasma produced in 2011.11 This increase may be in part due to the concern about transfusion-related acute lung injury (TRALI) and the exclusion of women who have been pregnant from plasma donation. Blood centers are attempting to make plasma from all eligible donors of the needed types, even though the plasma logistically cannot always be frozen within eight hours. More volunteer plasma is typically drawn than needed for transfusion. Plasma stored for as long as 72 hours before freezing may be sold for fractionation (discussed further in this chapter).

After separation from the RBCs, plasma may be pooled and treated with solvent and detergent (S/D) to decrease the risk of transfusion-transmitted disease. In addition, the pooling enables quality control of coagulation factors per lot, and the dilution dramatically decreases the risk of TRALI.68,69 Other pathogen reduction techniques may be applied (see Chapter 56). Only a small amount of S/D-treated plasma is used in the United States due to political and economic factors, and possible safety concerns regarding pooled products.68 However, some countries in Europe rely on this process for the majority of plasma transfused.68

Preparation of cryoprecipitate involves thawing frozen plasma at 4 °C in a circulating water bath, followed by centrifugation so that the supernatant plasma can be drained into an integrally attached storage bag (see Chapter 26). The remaining cold-precipitated material is then refrozen at ≤−18 °C and stored for up to 1 year. Approximately 1.7 million units of cryoprecipitate were prepared in the United States in 2011, an increase of 16% since 2008.11 In some regions in Europe, cryoprecipitate is not produced, as the use of factor concentrates for inherited bleeding disorders and plasma or fibrinogen concentrate for hypofibrinogenemia has proven satisfactory.

Leukocyte reduction is accomplished by passing whole blood or RBCs through filters that reduce the number of white blood cells (WBCs) (see Chapter 24). Ideally, this should be done as soon after collection as possible, but no longer than 72 hours. Leukoreduction has been shown to be more effective when done before storage because some of the adverse effects of transfusion are caused by factors produced or released by leukocytes during storage. Although leukocyte reduction can reduce untoward events, significant amounts of WBCs still remain in leukoreduced products (up to 5 × 10⁷ WBCs/unit in the United States and 1 × 10⁶ in Europe). Automated apheresis collections often have technology that produces leukocyte-reduced products during the collection process.
Automated collection
Over the first decade of the 21st century, advances in technology combined with a desire to optimize donations have led to a dramatic increase in automated collection of blood components. The collection of single-donor platelets using apheresis has increased coincident with the greater availability of automation and implementation of automated testing of platelet products. In 2011, 91.1% of platelets produced in the United States were from automated collection, up from 83.7% in 2008 and 67.7% in 2001.11 Eight of 30 European countries reporting for the same year collected >50% of their platelets by apheresis (the United Kingdom was the highest at 83%).70

Choice of which automated product(s) to collect depends on a number of factors, including blood type, height, weight, sex, risk of having antibodies that could cause TRALI, platelet count, hematocrit, the available collection technology, distance from manufacturing laboratories, and the time the donor has available to donate. Minimum donor qualification requirements for the various automated collection methods have developed historically—often independently. Therefore, some procedures have minimum requirements and length of deferrals that may differ from those of other procedures. A double RBC product is produced by an apheresis procedure where two units of RBC are collected at the same time, while returning donor plasma and often additional saline solution. In the United States, there is a 112-day deferral for donation of a double RBC product that also precludes platelet and plasma donation on some instrumentation. At the same time, a donor of a combined automated platelet, plasma, and RBC is deferred only 56 days for RBCs, but may often continue donating platelets and plasma again during the RBC deferral.

Product selection
Selection of which product(s) to draw from a given donor may be complex in a center with many choices. Obviously, the first concern is which product is most needed for patient care at that time. In addition, an underlying theme in blood banking is to maximize collection of universal donor AB plasma and universal donor group O RBCs. Many centers avoid collection of RBC units from group AB donors because many of these RBC units are wasted, since only AB recipients may use this blood. Recently, risk of antibodies that may cause TRALI has also disqualified donors from plasma and platelet donation who are at risk of having these antibodies. Finally, there may also be minimum height, weight, and hematocrit requirements that vary by technology and by sex. Therefore, a large male with a high platelet count might donate three units of platelets by apheresis, whereas a small woman who has TRALI risk might only donate an RBC unit.

With proper attention to donor interviewing and care of the donor, the blood donation process can be a pleasant and safe experience for the donor, while providing a safe and efficacious product to the recipient—the goal of the entire blood donation and transfusion chain.

Testing
Blood specimens drawn from the donor at the time of collection are sent for blood typing and infectious disease testing. Many hospitals that still collect their own blood find it more economical to send out the testing and receive the results electronically. Bacterial testing of platelet units is sometimes also done centrally.

ABO and RhD testing
Donor centers routinely test blood from each donation for ABO and RhD type (and K in some countries). “Forward” typing occurs by addition of antibody directed toward the A, B, and D antigens on donor red cells to obtain the blood type. “Reverse” grouping is performed by adding donor plasma to reagent red cells bearing A or B antigens to detect naturally occurring donor antibody to A and B. Algorithms ensure concordance of forward and reverse typing.

RhD is a special case (see Chapter 14). “Rh-negative” donors lacking RhD antigen undergo an additional step in the blood-screening process to determine if their cells possess the weak-D antigen. As a rule, when in doubt, blood centers err on the side of calling a donor RhD-positive, to avoid the chance of giving RhD-positive blood to an RhD-negative patient. At the transfusion service (recipient) level, the patient is typed, and, if in doubt, the transfusion service errs on the side of calling recipients RhD-negative, so they will not inadvertently be stimulated to make an alloantibody to D. The processes are optimized for these two divergent purposes. This is the reason that discrepancies may sometimes be discovered when blood donors become patients and their D typing may appear to change from positive in the blood donor setting to negative in the blood recipient setting.

Antibody screening
Donor plasma is also added to reagent red cells bearing an array of clinically significant RBC antigens. This is to screen for unexpected alloantibodies to epitopes in the Rh, Kell, Kidd, Duffy, and other antigen systems. Plasma from donors bearing alloantibodies is not used for transfusion; however, since RBCs contain so little plasma, these may be made available from donors with alloantibodies with the appropriate labeling. The screening of the donor for alloantibodies eliminates the need for the transfusion service to screen for donor antibodies to red cells and eliminates the need to perform a “minor” crossmatch (donor plasma mixed with patient red cells).

Infectious disease testing
Serological and nucleic acid testing for infectious disease is carried out in most high-income countries. The exact tests performed in a center depend on the incidence of the diseases in the population and also on availability of resources for testing (see Chapter 55). Testing requirements have changed frequently in recent years. Currently, infectious agents for which serologic screening is performed in the United States include human immunodeficiency virus-1 and -2 (HIV 1/2), hepatitis C virus (HCV), hepatitis B virus (HBV; HBV surface antigen [HBS-Ag] and HBV core [HBC]), human T-cell lymphotropic virus-1 and -2 (HTLV-I/II), Chagas disease, and syphilis. Nucleic acid amplification testing (NAAT) is performed for HIV 1/2, HCV, HBV, and West Nile virus. Supplemental or confirmatory testing is often done when licensed tests are available. This is useful for donor counseling and to potentially allow the donor to be eligible for a “reentry” protocol (which in the United States must conform to FDA guidance). In the United States, a donor is generally deferred even if the screening test is known to give a false-positive result. This is because the test has become uninformative for that donor (i.e., it cannot discriminate whether the donor has the disease). This often happens when blood-testing laboratories change from one testing platform to another (e.g., switching to a different instrument or reagent manufacturer). It is not unusual to have a higher number of deferrals concurrent with the implementation of the new technology due to the false-positive tests. Some countries—such as England—may be more donor centered in their testing algorithms. For instance, if a donor is
known to be false positive on a certain screening platform, subsequent specimens may be routed to an alternate platform, rather than deferring the donor. If a donor is known to have visited a malaria-endemic area, the donor might become eligible to donate after a short deferral period if a supplemental malaria test is performed, rather than be deferred as long as US donors. In 2011 in the United States, 1.1% of blood donors had abnormal disease marker results, resulting in a destruction of 102,000 units of blood.11

In addition to serological and nucleic acid testing of blood, bacterial culture is becoming widely used to test platelet products (see Chapter 53). Because platelets are stored at room temperature, rather than refrigerated or frozen, there is a greater chance that bacteria in the product might grow. These organisms may come from normal skin flora that contaminate the bag during phlebotomy, or they may be transiently circulating in the donor’s blood during collection.

Component modification and distribution
When a blood component has successfully completed processing, testing, and record review, then it is “labeled,” meaning that it has met all standards and is ready for infusion. Many countries have adopted ISBT 128, an identification system developed by the International Society of Blood Transfusion, that incorporates comprehensive barcode labels intended to set a global safety standard for the identification, labeling, and information processing of human blood, tissue, and organ products across international borders and disparate healthcare systems.21

The majority of a typical area’s blood supply is stored in hospitals for use when it is needed, rather than at the blood center. Availability and turnaround time are key components for determining allocations to each hospital; these depend on usage patterns and transportation distance from the blood center, and often the temperament of the clinical staff. Even a very small hospital that is a great distance from its blood supplier might have 10 or 20 units of RBCs on its shelves in preparation for the acute motor vehicle trauma that might occur every year or two. Unfortunately, this means that the vast majority of products shipped to this location will never be used. This leads to increased “outdating” of the products, and a disproportionally large effort to track the rotating inventory. Many blood centers monitor inventories in the hospitals. The center can then rotate out blood that may be expiring soon from the hospitals that use less blood to large hospitals and trauma centers that will be able to use the blood before expiration. In the United States in 2011, only 2.1% of allogeneic RBC donations outdated.11 The mean age of RBC units was 17.9 days at the time of transfusion.11 The low outdate rate suggests that blood centers have become more efficient at delivering the appropriate product when needed. However, when the expiration rate drops too low, then the safety margin of having enough blood at any particular time is reduced. The same year, 3.3% of US hospitals reported at least one day of cancelled elective surgeries due to blood inventory shortages, the lowest percentage reported since 1997.11

In the United States in 2011, 12% percent of transfused RBC units were modified by irradiation, an increase from 10% in 2008. Irradiation of platelets was higher: 46% of apheresis and 34% of whole blood–derived platelets were irradiated. At the same time, 53% of all transfused components were leukocyte reduced: 71% of RBC/whole blood, 80% of apheresis platelets, and 37% of whole blood–derived platelets.11 Leukoreduction in Europe remains variable. In 2011, 17 of 31 European countries responding to a survey used >95% leukoreduced blood.20

Plasma that is separated during component preparation and not needed for patient use becomes “recovered” plasma, and it is often used to supplement the supply of source plasma, as discussed in the “The Collection Process for Source Plasma” section.

Autologous and directed donation
The volunteer donor collection process also facilitates the collection of nonvolunteer blood donations. Many of the processes are similar. Autologous blood donation is the donation of one or more units of blood to oneself, usually in the preoperative setting. This practice rose in the 1980s and 1990s chiefly in response to concern over the risk of transfusion-transmitted viral infections. Since that time, preoperative autologous blood donation has been in decline while viral marker testing has improved significantly.22 Many other factors have converged to contribute to this downward trend in autologous blood donation, including recognition of the high cost, increased waste, and risk when compared to allogeneic blood donation, as well as the widespread adoption of patient blood management. Figure 4.3 illustrates the decreasing collection of autologous blood over the past decade in the United States.

A study published in the New England Journal of Medicine reported that the additional cost of autologous blood ranged from $68 to $4783 per unit of blood and resulted in “little expected health benefit” based on quality-adjusted years of life saved,73 which may reach tens of millions of dollars.24 The increased cost of autologous blood donation is not only related to the increased labor involved in collecting and storing the units, because a significant percentage of autologous donation units that are donated are ultimately discarded. A randomized study of preoperative autologous donation prior to hip surgery found that

![Figure 4.3 Autologous RBC units drawn in the United States by year. Note the dramatic decline after the maximum reached in 1992 (greater than a 21-fold decrease). The data are taken from the 2011 National Blood Collection and Utilization Survey.11 The points indicated by asterisks (*) have been extrapolated from cumulative member data supplied by Blood Centers of America (courtesy of Bill Block). Graphic design by Joshua E. Crookston.](image-url)
41% of the autologous units donated were not transfused. The choice of autologous blood donation has in the past been guided by the perceived increased risk associated with allogenic blood transfusion. However, the risk of transfusion-transmitted viral infection in the modern era of viral testing is lower than the risk associated with administrative error. Autologous blood donations have also been shown to be associated with an increased risk of developing adverse reactions when compared with the risks associated with donations from healthy volunteers. Finally, the concept of patient blood management has increasingly taken hold. This practice includes interventions that decrease the likelihood of transfusion, such as addressing anemia in the preoperative setting, intraoperative blood recovery, and restrictive use of transfusion overall.

Only 58% of the 113,000 autologous units collected in the United States in 2011 were transfused. This was a 59% decrease from 2008. The high outdate rate illustrates the high cost and inefficiency of autologous blood collection. These only accounted for <0.5% of all units transfused. Certain patients with rare blood types and alloantibodies that are difficult to match may benefit from autologous blood donation; however, it is not indicated for most transfusions. Some jurisdictions, such as the State of California, may require that a physician discuss the option of autologous blood donation when consenting patients for blood transfusion. However, clinicians may also point out that following a conservative transfusion practice and using allogenic blood only when needed remains the best choice for the majority of patients.

The collection process for source plasma: screening, phlebotomy, choice of product, collection, and testing of source plasma donors

The handling of source plasma donors differs in several respects from the handling of whole blood and apheresis donors providing blood products for hospital transfusion. Source plasma is collected by apheresis specifically for further manufacture into biological derivatives, in contrast to “recovered plasma,” which is the plasma remaining after RBC production from whole blood donation. About half of the recovered plasma collected for fractionation comes from Europe. Many European countries have maintained national programs that fractionate plasma from recovered plasma from volunteer donors. However, the demand for biological therapies worldwide requires the additional supply from remunerated or compensated (paid) donors. Source plasma is collected (in order of amount per population) in the United States, Austria, the Czech Republic, and Germany from compensated donors. Smaller programs are found for collections from noncompensated donors (in order of number per population) in Australia, the Netherlands, Denmark, France, Sweden, and Belgium and more recently Hungary. In 2010, source plasma accounted for approximately 75% of plasma for further manufacturing worldwide, with recovered plasma accounting for the remainder. In 2012, approximately 28 million L of source plasma was fractionated along with approximately 9 million L of recovered plasma. The number of collection centers in 2014 by Plasma Protein Therapeutics Association (PPTA) members was 467 and constantly increasing. US source plasma collections have been steadily increasing from more than 23.5 million L in 2011 to 26 million L in 2012 to 29 million L in 2013. The requirement for immune globulins have largely driven this increase (data from www.pptaglobal.org). The United States provides a large proportion of the world’s source plasma requirements for two reasons: First, under FDA regulations, source plasma donors can donate more plasma, more frequently, than is the case in most countries. Second, the United States has a well-developed source plasma industry that has invested in a network of centers that compensate donors for their time and inconvenience.

In both the United States and the European countries, source plasma is collected in fixed sites without mobile collections. Either the Autopheresis-C (Fresenius) or the PCS-2 (Haemometrics) is used for most collections. Recruitment is typically by word of mouth, newspapers, radio, and posters. The donor groups are heterogeneous. Sites near campuses that can attract student donors are common. Medium-sized cities and towns are favored over larger metropolitan areas. Payment varies between $25 and $50 for normal source plasma. More money is paid for donations from immunized donors for hyperimmune plasma (rabies immune plasma, tetanus immune plasma, hepatitis B immune plasma, anti-D plasma, etc.) and by those from donors with disease-state antibodies needed for diagnostic manufacture.

In addition to specific national regulations and guidance, in the United States and Europe an International Quality Plasma Program (IQPP) of the PPTA is also followed. The program has been judged successful because the major manufacturers in Europe and the United States will only use plasma from these programs. This self-regulation includes the following:

- **Community-based donors:** Donors must have a permanent address in the vicinity of the center.
- **Qualified donor standard:** Each donor’s plasma is used only after two medical screenings and required viral testings are successful and less than six months has elapsed between the two donations.
- **National Donor Deferral Registry (NDDR):** All donors deferred for viral marker testing are entered into an NDDR that must be checked before each applicant (i.e., not qualified) donor is accepted.
- **Viral marker standard:** This requires centers to keep their viral marker rates below established levels.
- **60-day inventory hold:** This is so that units from a donor with a subsequent positive test or disqualifying information can be removed before being pooled (part of the Q-SEAL Standards for fractionators).

The community-based donor standard discourages transient individuals from donating, as this population has been associated with an increased incidence of infectious disease markers. Under-the-nail photosensitive nail coloring is applied to ensure the donor only donates at one program at a time. A minimum weight of 50 kg (110 lbs.) must be met. At each donation, the hematocrit and total protein are determined from a fingerstick blood sample. The hematocrit must be 38% or greater (recently increased by FDA to 39% for males), and protein 6.0 g/dL or greater. The protein is measured using a refractometer (the only device currently available to meet the FDA requirement).

Initially, the donor is subjected to an extensive interview similar to that used for blood donors, followed by physical examination by a physician. In the United States, a physician substitute may be used, such as a nurse, paramedic, or other health professional trained to do the physical exam and operating under the guidance of the center medical director. The physical examination consists of an external eye, ear, and nose exam, with an examination of the throat with a tongue blade and light. Lymph nodes in the neck area are palpated. Auscultation of the back and front of the chest for lung abnormalities is followed by auscultation of the heart. The abdomen is examined for liver and spleen enlargement. A...
short neurological and extremity review completes the examination. In some centers, a urine dipstick for protein and glucose is also performed. After passing these initial tests, the donor can donate as an applicant donor. Collected units are held until the donor has two successful donations without any positive infectious disease markers. If the donor does not return for the second donation, the plasma is considered an “orphan” unit and cannot be used for injectable product. The donor must pass initially, and every four months, tests that include serum protein electrophoresis, total protein, and syphilis. The physical examination with full interview is repeated annually or if the donor has not presented in the past six months. An informed consent must be executed on the first donation and again whenever the consent is changed.

The donor donates according to a nomogram: body weights of 50–67.5, 68–79, and greater than 79 kg can donate 625, 750, and 800 ml plasma, respectively, not counting anticoagulant. Some centers infuse saline at the end of the donation. After a brief rest in the donation chair, the donor is allowed to collect the compensation (usually electronically added to a debit card) and leave. Refreshment and recovery areas are not common in plasma donor centers. In the United States, donors are allowed to donate no more than twice in seven days, with at least two days between donations. A donor could theoretically donate 104 times per year (65–83 L, depending on donor weight). The Council of Europe recommendations limit the amount of plasma collected per session to 600 mL, not counting anticoagulant. There is also a 15 L annual limit. German national guidelines set in 1999 allowed donations of up to 650 ml plasma twice weekly with an annual limit of 25 L. Donors must weigh a minimum of 50 kg and have a hemoglobin level of 12.5 g/dL in females and 13.5 g/dL in males. Immunoglobulin G (IgG) is measured at every 15th session to 600 mL, not counting anticoagulant. There is also a 15 L annual limit. German national guidelines set in 1999 allowed donations of up to 650 ml plasma twice weekly with an annual limit of 25 L. Donors must weigh a minimum of 50 kg and have a hemoglobin level of 12.5 g/dL in females and 13.5 g/dL in males. Immunoglobulin G (IgG) is measured at every 15th session.

To determine if less restrictive donation standards (closer to those in the United States) were safe, 21 German plasma donor centers participated in a study known as SIPLA. They found that donors weighing greater than 70 kg could donate 850 mL each session up to 60 times per year with appropriate monitoring (up to 51 L total per year). Currently, there is an effort to change European requirements to be consistent with these findings.

Each donation by a source plasma donor is tested serologically for HIV antibody, HBS-Ag, and hepatitis C antibody. Nucleic acid testing is done on each donation for HBV, HCV, and HIV. A positive test result in deferral. This is usually regardless of results of confirmatory tests that are performed for donor counseling. In addition, tests for hepatitis A and parvovirus are also performed. If positive, the units are discarded, but donor status is not affected and there is no counseling.

Due to the investment in the applicant’s first donation, donor centers cultivate long-term donors who donate often. Some very dedicated donors are given vaccines to provide rabies immune plasma, tetanus immune plasma, hepatitis B, or other immune plasma in order to make specialty immunoglobulins. Rh-negative donors who are not of childbearing potential can become donors of Rh-immune plasma for manufacture into Rh immune globulin. This is done by immunization with carefully “qualified” D-positive red cells. Long-term consistent donation is particularly important for these specialty donors.

There are additional requirements for donors receiving red cell immunizations, including physician performance of the initial physical examination and a separate informed consent, physician presence when immunizations are given, and a specific physician approval of the red cells to be injected. Meticulous preparation of the red cells for immunization occurs. Red cells from whole blood donors are frozen and collected over a year. Only when a year’s viral marker testing remains negative can the cells be deglycerolized and used to immunize a donor. When the red cells from a specific whole blood donor are first used, they are given to 1–3 recipients for a year. When viral marker testing is negative throughout the year for those recipients as well as the donor, the cells are then “qualified.” Plasma from these donors is used to manufacture Rh immune globulin, and the pool must contain a sufficient concentration (titer) of antibody to allow acceptable product to be made.

Rates of viral marker test positivity in donors are monitored, and plasma centers are expected to take steps to reduce levels when they rise above predetermined alert levels. Source plasma donors tend to be more likely male, younger, and larger in size than volunteer donors, probably reflecting the more demanding donation program frequency. In addition, they are more ethnically diverse. Some of these factors act to increase prevalence and incidence of viral diseases. Socioeconomic status and compensation programs might play a role as well. With the push toward voluntary donations worldwide, the payment of plasma donors has been criticized. Nevertheless, monetary compensation of source plasma donors has had an enviable safety record for the last 15 years since many of the additional controls have been put in place. The viral reduction and inactivation treatment of the final product provides additional safety. Thus, the layers of protection operate differently in source plasma programs than in the volunteer programs, but are still highly effective in preventing infectious units from entering plasma pools and in assuring safety of the final product.

The blood collection and transfusion chain is heterogeneous
In summary, the recruitment and screening of donors and the collection, processing, and testing of blood have developed dramatically over the past half-century. The blood donation and transfusion chain describes a highly regulated and technology-rich field. Much of the global blood supply is collected by procurement agencies that may differ greatly in structure and organization. Systems that are very different may still be successful in collecting and delivering a beneficial, life-saving product to patients when they need it. At the same time, the disparity between resources used in high-income countries and low-income countries for procurement of safe blood is perhaps greater than in any other area of healthcare.

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