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It is estimated that each year more than 81 million units of blood are collected worldwide, but the availability of this blood for medical use is not evenly distributed across the globe. The average number of blood donations per 1000 population is 12 times greater in high-income countries and 3 times greater in medium-income countries than in low-income countries (WHO, 2005a). Only about 27 million of the 81 million units (approximately 33 percent) are collected in low- and medium-income countries, where 82 percent of the world’s population resides. In developed nations about one patient in ten admitted to the hospital receives blood or some type of blood product, while in developing countries the number is much smaller because of financial constraints, limited access to advanced medical procedures, and a lack of a modern, effective blood-banking system. It is estimated that 70 percent of blood transfusions in Africa go to children with malaria and to treat women with post-partum hemorrhage, and that perhaps 100,000 people die annually because of unsafe transfusion practices (Heyns et al., 2005). Still, the demand grows for safe blood products in developing nations.

About 8 million people in the United States voluntarily donate about 12 million units of blood each year. These units are then processed into about 20 million units of blood components, such as red blood cells, platelet, and plasma units (The National Blood Data Resource Center of the United States, 2005; US General Services, Administration, 2006). Modern medical care would not be possible without a safe and dependable blood supply to treat leukemia and certain cancers; to perform complex surgical procedures like heart operations, liver transplants and joint replacement; and to treat blood diseases like sickle cell anemia and thalassemia. Blood replacement is essential in acute trauma care, including accidents, burns, and battlefield injuries. The demand for blood is also growing in response to the world’s aging demographics – for example, in the United States people over the age of 69 make up about 10 percent of the population, but receive about 50 percent of components.
This chapter is primarily about components of volunteer blood donations that are each transfused as a single unit, usually “as is.” A single donation of a pint of whole blood is virtually always separated by centrifugation into a unit of red blood cells and a unit of plasma; a unit of platelets or a unit of cryoprecipitated plasma can also be prepared, but this is done for less than half of whole blood donations, since patients’ clinical needs for platelets and cryoprecipitated plasma are much less than patients’ needs for red blood cell transfusion. Each of these units is labeled, and regulated as a drug, following FDA regulations. While today virtually all of these blood components from whole blood donation are from volunteer donors, the FDA would permit paying these donors, but requires that the component’s label be marked conspicuously with the words “PAID DONOR” as opposed to “VOLUNTEER DONOR.” Whole blood donation is permitted no more often than once every eight weeks (to prevent development of iron deficiency in the donor).

Most of the plasma separated from red blood cell units is not needed for direct transfusion to patients, and so it is provided as “Recovered Plasma” to large multi-national for-profit companies that pool and fractionate it into plasma derivatives. The major source of plasma for plasma derivative manufacture, however, is “Source Plasma” collected by plasmapheresis (not whole blood collection). In the US, as well as many other countries, this Source Plasma is collected from donors who are paid (i.e. not volunteer), and the units of Source Plasma are labeled “Paid Donor.” Plasmapheresis today is an automated procedure in which blood is removed from a donor, and the red cells are returned but the plasma is retained outside the body. Donors may undergo this procedure as often as twice a week. Source Plasma from tens of thousands of donations is pooled by the plasma fractionators who then, utilizing a series of complex processes, chemically and physically separate the plasma into lots of several plasma derivatives, including albumin, gamma globulin, and sometimes Factor VIII and Factor IX concentrates (used in developing parts of the world to treat patients with hemophilia A and B respectively), as well as alpha 1 anti-trypsin. Currently, the process of plasma fractionation includes several purifying and sterilizing steps which render these derivatives essentially safe, even though the source material is from pools of plasma from thousands of paid donors (each donation is, though, still tested for hepatitis B and C, as well as HIV). Prior to the availability of HIV and hepatitis C testing, and prior to the addition of sterilizing steps in plasma fractionation in the 1980s, large numbers of patients with hemophilia were regularly exposed to hepatitis C and HIV, which resulted in a number of national scandals and law suits (see p. 208: Negligence, human error, and failed oversight). Today in the US most patients with hemophilia A and B are treated with synthetic preparations of Factor VIII and Factor IX (respectively), which are viewed as essentially virally safe but also much more expensive. The sterilizing steps used in plasma fractionation are not suited to the single blood components used for direct transfusion, since these processes would damage red blood cells, platelets, and whole plasma, such that these components would not be efficacious.
Testing of blood donations for infectivity is viewed as part of the manufacturing process for the pharmaceutical drug (red blood cells, platelets, or plasma), and the test is to “determine the suitability for human use” of the blood component. This is the “purpose” for this testing, rather than for making a clinical diagnosis in the person donating the blood (who is presumed to be healthy and not a “patient”) or screening the blood donor population for syphilis or HIV. Accordingly, it is very important that the false-negative rate in testing be as low as it can be (to prevent disease transmission by transfusion) — this would be good “sensitivity.” However in doing this, the false-positive rate increases — this would be bad “specificity.” Since there is a false-positive rate, and since blood centers view it as their obligation to inform donors of unsuitable test results, even false-positive test results make donors ineligible for subsequent blood donation. More important, though, is for donors to know if they are truly positive, in which case counseling is required to prevent future transmission to others (e.g. to sex partners), and referral to a health-care facility to initiate treatment, if appropriate, is required. It is therefore important that there be a “confirmatory” test to complement each reactive screening test result. To use anti-HIV testing as an example, the screening assay is an automated enzyme-linked immunoassay (EIA); if the EIA is repeatedly reactive then the donor is deferred in any event, but a Western blot (the confirmatory assay) is performed; if the WB is positive, the donor is considered infected and needs to be counseled to avoid exposing others, and to seek treatment for HIV. The more difficult counseling, however, is of the donor whose screening assay is repeat-reactive and whose confirmatory assay is negative — a false positive. This person is healthy and not infected, but is not permitted to donate blood any more (by federal regulation; there are complicated “re-entry” algorithms available which some blood centers use).

As we shall discuss, the social ecology for maintaining a safe blood supply is complex, but one point cannot be overemphasized: voluntary donation is its cornerstone. Where blood is in short supply and nations are poor, it is common to pay donors. Time and again this practice has been shown to increase the risk of introducing potentially lethal infectious agents. To date, the Government of Malawi is one of only a few in developing nations to establish a national voluntary blood donation system. It took two years to set up the system and its benefits were rapidly seen: the death rate from malarial anemia dropped by 60 percent and pregnancy-related mortality fell by more than 50 percent (Heyns et al., 2005). Even with a purely voluntary donor system, blood must be screened for transmissible infectious agents. The strategies for optimal screening are based on the human social environment, which include factors related to demography, behavior, and geography. For example, in South Africa and Zimbabwe it is estimated that the overall rate of HIV infection is greater than 20 percent of the population. Based on the risk factors known to be associated with HIV transmission, both countries instituted appropriate donor-screening procedures and reduced the rate of HIV positivity in blood donations to below 0.5 percent (and these units
are discarded, not used). This has not been accomplished throughout sub Saharan Africa. The World Health Organization (WHO) estimates that HIV-contaminated blood still accounts for 5 percent of HIV infections throughout the region (Heyns et al., 2005).

A brief history of improving blood safety

In 1937, Dr Bernard Fantus established the first blood bank in the United States at Cook County Hospital in Chicago. He is also credited with coining the term “blood bank” to describe a laboratory capable of preserving and storing blood. In just a few years, blood-banking spread across the United States and Europe. In 1940 the process of fractionation for breaking down plasma into albumin and gamma globulin was discovered, and these products soon were available for clinical use. World War II created an immediate demand for blood, and around this time the American Red Cross started using the vacuum bottle to collect and store donated blood. Whole blood donations were tested for ABO and Rh type, as well as syphilis. Meanwhile, the United States Government set up a nationwide program for collecting blood, and the “Plasma for Britain” program to aid the British war effort. During the war, albumin was used to treat shock, the Coombs test was discovered, and acid citrate dextrose (ACD) solution came into use to prolong shelf-life – thereby making more blood available for transfusion.

During World War II and the succeeding years, blood centers were established across the United States and other developed nations. The American Association of Blood Banks (AABB) was established in 1947, with a mission to promote safe blood-banking and improve public and professional education. Fueled by advances in medical care, like open-heart surgery and trauma care, there was steady increase in the demand for blood during the 1950s. In 1970, component therapy came into medical practice – first with red blood cells and plasma, and later with platelets and cryoprecipitated antihemophilic factor (AHF) for transfusion. Today, blood is transfused to a patient essentially only as one of the components of whole blood – i.e. red cells, platelets, or plasma – while whole blood is rarely transfused as such. This approach is beneficial in two respects: it is clinically better for the individual patient to receive only the component needed (and not be exposed to potential adverse effects of the other, unrelated component), and it also permits several patients to benefit from each unit of donated whole blood. In addition, the optimal storage conditions are different for the different blood components – red cells are refrigerated, plasma is frozen, and platelets are agitated at room temperature. Up to four different components may be derived from one unit of blood, but nowadays rarely more than three are prepared.

Giving blood is relatively painless and, in all but very rare circumstances, free of serious adverse consequences. The fluid lost is usually replaced naturally within 24 hours, but it can take up to two months to replace the lost red blood
cells. Whole blood can be donated once every eight weeks (56 days). Multiple units of platelets can be collected as frequently as every two weeks by a procedure called platelet pheresis. Two or three units of plasma can be collected at a time by plasmapheresis, even more frequently. However, two units of red blood cells can safely be donated only once every 16 weeks, also by plasmapheresis.

Over the past four decades there has been enormous improvement in the safety of the blood supply. From 1970 to 2000, the overall risk of acquiring a transfusion-transmitted infection in the United States dropped from one in 70,000 to one in 11.15 million units transfused. This is mirrored in the risk of acquiring specific infectious agents, like hepatitis B and C – for example, from 1970 to 1999 the risk of acquiring hepatitis B virus dropped from 1:855 to 1:138,700 units transfused (Dodd, 2001). Table 7.1 illustrates the risk of acquiring HBV between 1970 and 1999, and Table 7.2 illustrates current estimated risk of acquiring HIV, hepatitis B and C, and HTLV I and II via transfusion. Table 7.3 estimates the risk of acquiring these agents, comparing it with other life risks such as sports, accidents, and other illnesses.

Table 7.1 Risk of transfusion-related hepatitis B infection

| Year | Risk/unit | Comment                  |
|------|-----------|--------------------------|
| 1970 | 1:855     | Based on CEP rate        |
| 1979 | 1:562     | TTV study                |
| 1979 | 1:2809    | TTV (today’s tests)      |
| 1995 | 1:250,000 | Test sensitivity         |
| 1996 | 1:63,000  | Window                   |
| 1999 | 1:138,700 | Window, 1989 incidence   |

Source: Adapted from Dodd (2001), with permission.

Table 7.2 Current transfusion risks*

| Agent          | Point estimate | 95% Confidence level |
|----------------|----------------|----------------------|
| HIV            | 1:493,000      | 1:202,000–1:2,778,000|
| Hepatitis B    | 1:63,000       | 1:31,000–1:147,000   |
| Hepatitis C    | 1:103,000      | 1:28,000–1:288,000   |
| HTLV I and II  | 1:641,000      | 1:256,000–1:2,000,000|

*Per unit of blood that is negative in laboratory testing. Adapted from Schreiber et al. (1996).
A person is far more likely to die in a motorcycle accident or from rock climbing than from receiving a blood transfusion. Until 1999 the tests for infectivity mainly involved measuring antibody to the virus. An important recent addition to blood safety came in 1999 with Nucleic Acid Amplification Testing (NAT), which employs a new technology that specifically can detect very small amounts of the genetic materials of viruses like HCV, HIV, and West Nile Virus (WNV).

### The social ecology of blood safety

Most infectious agents transmissible by transfusion have been around for many years, so in general it is prior donor activity that determines whether a unit of blood is infected or not. Occasionally a new microbe, like the human immunodeficiency virus (HIV) or Babesia microti, is introduced. And, while West Nile Virus may have been in Africa for some time, it was first identified only recently in the United States. Regardless whether it is an ancient or new agent,
similar human activities are likely to underpin their entry into and transmission along the medical blood supply. They include intravenous drug use with needle-sharing, high-risk or multiple partner sexual activity, exposure to insect vectors, travel, population migration, and medical negligence, and each may be influenced by economic, political, and social conditions. These subjects are discussed elsewhere in this volume, so this chapter will focus on their specific impact on blood safety.

By far the greatest challenge to blood safety today is in the developing world, primarily in sub-Saharan Africa and parts of Asia, as a consequence of inadequate resources and dated technology in the health sector. The result has been epidemics of transfusion-related HIV, hepatitis, and other infectious diseases. Failing to test all donated blood for infectious agents is thought to have caused up to 16 million HBV infections, 5 million HCV infections, and 160,000 cases of HIV worldwide (Heyns et al., 2005). In 1975, a World Health Assembly (WHA) resolution called for countries to adopt nationally coordinated, voluntary blood transfusion services. So far, fewer than 30 percent of the signatory states have done so. In contrast, developed nations have made a deliberate policy to ignore cost in order to emphasize safety. The result has been steady increases in transfusion safety and cost. In the United States, the Food and Drug Administration (USFDA) has been regulating blood-banking for several decades. However, around 1990 the FDA also started applying the regulations for pharmaceutical manufacture to blood-banking. Also, in its mission to protect the public health, it is not permitted to consider cost when promulgating rules and conducting oversight – so, even though proven not to be cost-effective, the FDA approved, on an interim basis, p-24 antigen testing for HIV. The FDA at the time was looking ahead to when a more effective NAT test would be available. Still, one study estimated it costs about $2 million to prevent one case of transfusion-related HIV (Heyns et al., 2005). Currently, NAT is routinely performed to detect HIV-1, hepatitis C Virus (HCV), and West Nile virus. Figure 7.1 illustrates the steady rise in the price of blood-banking services, due in part to increased testing. It should also be noted that in earlier years blood centers traditionally had underpriced the cost of providing red cells for transfusion.

The challenge is to make widespread testing commonplace in countries where cost is a limiting factor. Currently, advanced testing for HIV and HCV, and bacterial culture tests on platelets, are not available in most developing countries.

Effective public health strategies: incentives, education, screening and procedures

Relatively low-cost, low-technology public health strategies continue to be the first-line and most important defenses to protect blood safety. They include
establishing an altruistic system for blood donation, effective public education, rigorous professional training, and continuous epidemiological surveillance and consistent front-line screening (not testing) of prospective donors before they give blood. While the array of accurate laboratory screening tests continues to grow, it is probably fair to predict that there never will be a fully effective laboratory test for every infectious agent that can be transmitted via blood transfusion. The environment of infectious microbes is always changing, as is the ecology of human activities that can spread them. It is therefore realistic to expect that the next infectious agent will be present in asymptomatic blood donors before there is a test for it. Other sources of risk include the donor that is infectious but not yet positive by available testing; an infection that is immuno-silent; lab error; and the eruption of a new infectious agent or new variant of a known agent. With this reality in mind, continuous epidemiological surveillance to uncover changing disease patterns and a willingness to be creative, diligent, and rapid in adapting to new challenges are the keys to maintaining public health. In addition, as we learned from the outset of the AIDS epidemic, public health measures will have to adapt to ethical and legal parameters of pluralistic societies. The challenges to maintaining sufficient blood supplies for life-saving medical needs are constantly changing while demand is always increasing. Not long ago, there were concerns related to discriminating against vulnerable and stigmatized groups. Today, a concern is rejecting people that have traveled to or lived in Western Europe.

Figure 7.1 Graph of safety measures and mean red cell fees, 1985–2005. Reproduced with permission of America’s Blood Centers.

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The voluntary donor system

Voluntary donation continues to be the foundation for maintaining blood safety. To date, only about 40 countries in the world have established systems for fully voluntary blood donation. This includes only about half of the 52 WHO European Member States, with 17 more in the process of developing one (WHO, 2005b). The problem is primarily in Eastern Europe. Africa is less advanced, with only about 15 percent of the 46 Member States in the African Region having a voluntary system, and only 30 percent have plans on the table to institute such a policy. It is estimated that about 60 percent of transfusions come from family donors, who are known to be more likely than voluntary donors to have a transmissible infectious agent (WHO, 2002).

The United States has a fully voluntary system. Most collection centers in the United States stopped paying for blood in the late 1960s, and with that came a clear reduction in transmission of hepatitis by transfusion. In the early 1970s in the United States there was a risk of approximately 6–8 percent of contracting some form of hepatitis from a transfusion. The risk now of becoming infected with hepatitis B is about 1 in 250,000, and the risk of acquiring hepatitis C is less than 1 in 3300 units transfused. This remarkable improvement in reducing post-transfusion hepatitis may be considered a marker for overall blood safety that occurred from the mid-1960s onward with the US national shift to voluntary blood donation. To appreciate the role of voluntary donation in this improvement, it is helpful to note that at about this time Australia Antigen testing (HBsAg Assay) for hepatitis B was introduced. However, the Australian Antigen test does not detect hepatitis C (previously called Non A/Non B), and HCV transmission declined over these years. It seems reasonable to conclude that voluntary donation works. After 1970, only a very few institutions in the United States continued to pay certain blood donors, and the last few stopped the practice in the past 15 years. Since 2004, we believe that all blood components transfused in the US come from volunteer sources.

In summary, the most critical area for change is in the developing world, where well-established voluntary donor systems still do not exist. The consequence is a much higher rate of transfusion-related infection in these countries, due to agents like HIV, hepatitis B and C, and Chagas’ disease, where it is found only in the Americas (WHO, 2004). In response to this public health problem, the World Health Organization strongly advocates that “Member States promote national blood transfusion services, based on voluntary non-remunerated donations, and promulgate laws to govern their operation” (see also the May 1975 World Health Assembly resolution WHA 28.72). And the problem is not isolated to Africa. WHO Europe (2006) notes:

The spread of the HIV/AIDS epidemic makes this issue {voluntary donation} of primary concern for many countries of the WHO European Region. The latest data show that in Western Europe, where blood donations are mainly non-remunerated,
HIV prevalence has declined regularly over time to 1.3 per 100,000 donations (2002). In Eastern Europe, where the national blood supplies are mainly based on paid or family replacement donors, HIV prevalence has increased alarmingly during the last years, up to more than 40 times when compared to some Western European countries.

Public education and health screening

Another element in the first-line defense system is effective public education and health screening. In the United States, it is estimated that each year less than 5 percent of individuals eligible to donate blood actually do so. A donor must be in good health, weigh at least 110 pounds, and be at least 17 years of age (some states permit donors under the age of 17 with parental approval). Most blood banks have no upper age limit, and an increasing number of seniors give blood. Getting more voluntary donors requires appealing to both individual self-interest and community spirit. The American Red Cross public education message points out that most of us will “face a time of great vulnerability in which we will need blood. And that time is all too often unexpected” (American Red Cross, 2006a).

An effective public media campaign also involves educating individuals about the need for voluntary exclusion, so that people in a high-risk group or in poor health do not try to donate blood. At present in the United States, guidelines for ineligibility include (Food and Drug Administration, 2002):

- a prior history of illegal intravenous drug use
- a man who has had sexual contact with another man (MSM) since 1977; however, this is currently being reconsidered, the proposal being to accept MSM only if there has been no MSM activity in the last year
- any history of receiving clotting-factor concentrates
- a positive HIV test
- a history of engaging in sex for money or drugs since 1977
- a history of hepatitis since age 11
- a history of babesiosis or Chagas’ disease
- ever having taken Tegison for psoriasis
- risk factors for Creutzfeldt-Jakob disease (CJD), which include a family member with CJD, receipt of a dura mater transplant or administration of human pituitary derived growth hormone, and/or transmission via reusable instruments employed during brain surgery
- risk factors for variant Creutzfeldt-Jacob Disease or vCJD, which include three months or more spent in the United Kingdom from 1980 through 1996, or five years spent in Europe from 1980 to the present.

Public health prevention also includes identifying and refraining from collecting blood at high-risk locations, such as prisons and mental health facilities, where
there is a high-risk for hepatitis; and, even though there is an effective test for HIV contamination, avoiding community settings with a relatively high concentration of men who have sex with men, because of the risk of HIV infection. To some, this policy is controversial.

Educational materials provided in advance contain clear and specific instructions that list the exclusions for giving blood, such as recent travel to a geographic location where malaria is endemic, or residence in Europe where variant Creutzfeldt-Jacob Disease (vCJD) is present (see below). Upon entering the blood collection center, prospective donors are given written materials with information on the risks and symptoms associated with infectious diseases transmitted by blood transfusion. They are asked questions and then given a form to sign indicating they have read and understood the material, and have provided accurate personal information. Questions also are asked about donor safety, such as a medical history of heart disease, current fever, or other sign of infectious disease. At that point, they can elect to leave without giving blood.

Donors then are asked clear and specific questions about behaviors that increase the risk of carrying an infectious agent that can be transmitted by transfusion, such as injecting drugs, sexual activity, recent tattooing, and travel. These questions are updated as needed to account for changing infectious disease epidemiology. For example, in response to the newly emerging AIDS epidemic of the early 1980s, blood collection centers began asking men about sexual contact with other men. Even though a virus had not yet been isolated and determined to cause AIDS, population-based data were showing the new disease to be behaving like hepatitis B, which already was well known to be caused by a virus and spread by sexual activity, by sharing intravenous needles during recreational drug use, and by blood transfusion. In general, the public health approach is to continue an effective screening measure until population-based data points conclusively in another direction. It is rare to discontinue the strict application of a screening protocol until there is convincing data over a sustained period of time. Thus, it was several years before Haitians in the United States stopped being considered a separate risk group for HIV.

In the United States, the policy generally is to screen for individual behavior, not group ethnicity. The first instructions for identifying AIDS were promulgated in January 1983. In March 1985, a laboratory test became available to screen for HIV in donated blood. The test was developed within a year, and was made available for donor screening prior to large-scale experience with the screening test and its confirmatory test, the Western Blot. Accordingly, as experience developed, with millions of blood donations being tested, information regarding the false-positive rate became available and the test was modified over the next few years to improve its specificity. Still, the screening questions were not changed until solid epidemiological information became available. To do this, donors with positive test results were interviewed and specific criteria for Western Blot positivity began to be developed by looking at individuals who had
been considered Western Blot-positive but had no risk factors for disease. Then the exclusion policy was revised to ask donors specific questions about behavior. Guidelines recently were revised for tattooing, now done on a state-by-state basis based on each state’s own regulation of tattooing facilities.

**Epidemiological surveillance**

Each month, the American Red Cross monitors the true positive rate of each of its infectious disease markers. Since the beginning of HIV testing, there has been a clear downward trend in units that confirm positive for HIV (Dodd, 1994). This reflects improvement in donor screening. There has also been new and more active coordination between agencies and organizations through weekly surveillance of West Nile Virus positivity in blood donors. This positivity actually precedes the CDC’s identification of human cases of West Nile Virus disease, so in this situation the coordination of blood-banking and general epidemiology has positive synergistic impacts for public health. Since all positive tests on blood donors are followed up individually by the local blood region, a local increase in confirmed positives suggesting a local epidemic can then be further followed up by local public health entities. And local public health departments notify the local Red Cross about changes in disease epidemiology, so blood collection centers can refrain from blood collection drives in potential epidemic situations.

**Laboratory testing**

In the past 15 years there has been a proliferation of new and better laboratory tests for infectious diseases that can be transmitted by transfusion. Before 1985, blood products were tested only for antibodies to *Treponema pallidum* (the bacterium that causes syphilis), and the Australian Antigen for hepatitis B surface antigen (HBsAg). Additional tests were developed for hepatitis B and C, HIV 1 and 2, and HTLV-I. Testing for parasites has been discussed for many years, but the FDA has yet to license a test to screen for malaria or Chagas’ disease. With the risk of contamination from viral agents diminished, there is now a greater emphasis on developing assays for parasites.

In the United States, the policy is to screen each unit of blood as soon as a new assay is licensed; this currently includes the following laboratory tests (see Table 7.4):

- syphilis
- hepatitis B (HBV)
- hepatitis C (HCV)
- human immunodeficiency virus (HIV-1 and HIV-2)
- human T-lymphotropic virus (HTLV-I and -II)
West Nile Virus (WNV)

- Testing of platelet donations for bacterial contamination.

Once approved, a laboratory test will be conducted on all donations until either a new and better test is licensed, or population-based data indicate that it is no longer productive. For example, ALT testing for hepatitis continued until 2003, and was discontinued only when a more specific and sensitive test became available to detect HCV. Similarly, HIV p24 antigen testing was discontinued in 2003, but only when a specific and sensitive nucleic acid amplification test (NAT) was licensed for HIV1 and added to routine donor screening. From 15 March 1996 to 27 March 1999, HIV-1 p24 antigen testing was performed on approximately 45,000,000 units. Even with additional neutralization testing, there were many false-positive test results. Still, testing continued, and during this period only five donors were found to be HIV-antigen positive and HIV-antibody negative – which was about 1 in 9 million units tested. Currently, the United States is the only
country to test for HIV-RNA (the United Kingdom and others test for HCV-RNA, but not for HIV-RNA). It is estimated that RNA testing reduces the risk of HIV and HCV transmission to about 1 in 2 million blood units.

It should be noted that there can be a difference between a laboratory test available for blood testing, and that licensed for the clinical assessment of patients. For example, there are diagnostic clinical tests for Chagas’ disease and malaria, but still none licensed for screening blood. In contrast, the laboratory test for anti-HIV1 was licensed for blood-donor screening before it was approved for patient use.

High-risk human behavior

On 13 May 1981, John Paul II was shot and critically wounded in an assassination attempt. During the five-hour surgical procedure at a Rome hospital to repair his wounds, the Pope was given six pints of blood. On 20 June 1981, he was hospitalized with a high fever and inflammation of the right lung. The Pope was tested and found to be infected with cytomegalovirus (CMV), a herpes-type virus that can be transmitted by sexual contact and blood transfusion. He had acquired CMV from the blood administered during surgery. At the time, neither Italian law nor standard medical practice required the transfused units to be tested for CMV (Catholic News Service, 2005). A number of years later, filtering the white blood cells’ blood components came into common use, which reduces the risk of CMV from transfusion. Pope John Paul’s experience illustrates the link between human behavior and transfusion risk. There are a number of infectious agents associated with human high-risk sexual behavior and injecting drug use that are of special concern for safety of the blood supply. The first to be identified was syphilis, for which testing began just after World War II, at a time when the rate of syphilis infection was much higher in the general population. Then and now, however, the risk of acquiring syphilis via blood transfusion, if present at all, is exceedingly small – in fact, in the United States there have been no recorded cases transmitted by transfusion in many years, and only one report in the literature (in the 1970s) of a poorly documented case of syphilis transmitted by transfusion. Moreover, the spirochete that causes syphilis is fragile and becomes inactive during the first few days of refrigerated blood storage. The same cannot be said for hepatitis B, HIV, HTLV, and CMV, however, as these infections are spread sexually and can also be transmitted by transfusion.

Impact of injection drug use and sexual activity

Since it was recognized in late 1982 that blood transfusions could transmit HIV, there has been increased international attention on the link between sexual activity,
injecting illicit drugs, and blood safety. Epidemics related to high-risk sexual activity, such as sex work and trading sex for drugs, are discussed in Chapter 2, and epidemics related to intravenous drug use are discussed in Chapter 3. Both types of behavior are known to impact the safety of the blood supply, especially when donors are paid. Blood is an ideal medium for harboring, growing, and transmitting the agents that are spread by these behaviors, such as HIV, the hepatitis B and C viruses, HTLV, CMV, and others. To combat this problem, the Federation of Red Cross and Red Crescent Societies has called for expanded drug abuse prevention, harm reduction, and public education. They believe that “National Societies, with their unique combination of volunteer support and community membership alongside their status as auxiliaries to the public authorities in the humanitarian field, have a special contribution to make to the best approach to the challenges at the national and community level” (Kopketzky, 2005). For more than two decades international attention has been on the AIDS epidemic, where HIV, like the hepatitis B virus, is known to spread by sexual contact and IVDU. Of note is that five countries in the former Soviet Union and Asia that have combined populations of almost 2 billion are seeing HIV epidemics of more than 50,000 registered cases per country (Wolfe and Malinowska-Sempruch, 2007). These epidemics are associated with high-risk human sexual activity and injection drug use, and these nations also have limited safety controls on blood banking. Even with improved laboratory screening, the front-line defense in these states, as in developed nations, is effective public health screening. The US guidelines that relate most directly to uncovering high-risk sexual activity and IVDU also exclude any individual with AIDS or a positive HIV test. In addition, they exclude individuals that have:

- a history of injecting illicit drugs, including steroids and other medications not prescribed by a physician
- any man who since 1977 has had sex with another man, even once
- anyone who since 1977 who has ever taken money, drugs, or other payment for sex
- anyone who since 1977 was born in, lived in, or received a transfusion or medical treatment in Cameroon, Central African Republic, Chad, Congo, Equatorial Guinea, Gabon, Niger, or Nigeria, or had sexual contact in the past 12 months with anyone described above.

Type O is a rare form of HIV found primarily in West Africa. As of this writing, there is no laboratory test approved in the United States to detect Type O in donated blood. In 1996, the United States Food and Drug Administration promulgated rules that prohibit blood donation by individuals born in these West African States after 1977, and persons that have had sexual contact with someone born in one of these nations since 1977.
Impact of migration, travel, and geography

While travel, migration, and trade are expanding rapidly over the globe, the movement between countries of blood components for transfusion is still relatively uncommon, and to date the blood supply of developed nations has remained remarkably immune from infection by travel and migration. For example, it is estimated that 300–500 million people have malaria, but perhaps only a handful of cases each year in the United States are due to infection via the blood supply. Similarly, while Chagas’ disease is endemic in Mexico, Central and South America, and millions of people from these countries travel annually to America, the reported incidence of Chagas’ disease due to blood transfusion in the United States is very, very low (Chamberland et al., 1998). Nevertheless, concern is real because blood is an extraordinarily effective vehicle for transmitting infectious agents (Chamberland et al., 1998). Since a fully effective laboratory test for every blood-transmissible infectious disease in the world is not on the horizon, the current first line of defense will have to remain effective health screening and public education before individuals give blood. It also is hopeful to note that new laboratory tests to screen human blood are being developed. As noted already, in the wake of improved screening tests for infections transmissible by transfusion, we are seeing a greater emphasis on developing screens for parasites (e.g. Chagas’ disease and malaria) that can infect the blood supply. Even with these population shifts, the blood supply in developed nations remains remarkably safe, as illustrated in Table 7.5, which shows the low rate of transfusion-related infection due to malaria and to T. cruzi infections not endemic in the United States, as well as babesiosis, which is endemic in the US.

| Agent   | Frequency per million units (per actual unit) | Clinical disease       |
|---------|---------------------------------------------|------------------------|
|         |                                             | Acute per million units | Chronic per million units | Deaths per million units |
| Babesia | >1/100,000                                   | 1.0                    | 0                        | 0.25                    |
| Malaria | >1/250,000                                   | 4.0                    | 0                        | 0.00                    |
| T. cruzi| 24–80/1/12,500–1/50,000                      | 0.0–1.0                | 0                        | 0.00                    |

Source: Adapted from Dodd (1994).
Malaria

Between 1958 and 1998, the Centers for Disease Control recorded 103 cases of transfusion-transmitted malaria in the United States. Malaria is not endemic in North America, so these cases most likely were the result of blood donated by people who were asymptomatic carriers. In the United States, potential donors are screened by questionnaire and asked to refrain from giving blood until one year after visiting a malarial area, three years after completing treatment for malaria, or three years after living in an area where it is endemic. While very rare in the US, malaria is epidemic in tropical areas and causes serious health consequences, including death. There is no practical test available to screen donors. Table 7.5 illustrates that the US estimate of malaria contamination to the blood supply currently is small, at about just over 1/250,000 units with no fatalities. However, the problem is wholly different in tropical countries, particularly in sub Saharan Africa. Worldwide malaria is the most significant cause of death due to parasitic infection. The World Health Organization estimates there are at least 300 million acute cases of malaria each year globally, which lead to more than a million deaths. Probably 90 percent of the deaths occur in Africa, mostly in young children. Blood transfusion is used to treat life-threatening malaria in young children, but also poses the risk of acquiring HIV infection (Obonyo et al., 1998; WHO, 2006a).

Creutzfeldt-Jacob Disease (CJD) and variant Creutzfeldt-Jacob Disease (vCJD)

CJD is a rare degenerative, fatal disorder of the central nervous system. Worldwide, its incidence is about one person per million per year. CJD can affect humans in three ways: sporadic CJD, which has no known risk factors and accounts for 85 percent of CJD cases; hereditary CJD, which occurs in individuals with a family history of the disease and tests positive for specific genetic mutations; and acquired CJD, which is transmitted by exposure to brain or nervous system tissue. Acquired CJD accounts for less than 1 percent of CJD cases, and has occurred most in individuals that received repeated injections of human pituitary gland growth hormone. This preparation was prepared from pools of pituitary glands from a number of cadavers. Through the 1950s it was used to treat congenital dwarfism, although this practice was subsequently supplanted by a synthetic growth hormone preparation. CJD also has been transmitted to patients who have undergone brain surgery, including transplant of the dura mater – the covering of the brain and spinal cord. This material was harvested from human cadavers and then used in some brain operations. The dura mater had been stored in a vat along with dura mater from other cadavers that had contaminated material. Affected individuals may take decades to develop symptoms,
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and then progress rapidly to dementia, severe loss of coordination, and death. While the cause of CJD remains uncertain, the suspicion now is that it occurs in response to abnormal changes in the shape of brain prions. Currently, there is no screening test for the disease, and while blood transfusions have never been shown to transmit CJD, as a precaution the Food and Drug Administration (FDA) prohibits blood donation by individuals who may be at risk. These include potential donors who have received injections of human-derived pituitary hormone, those with a family history of CJD, or those who have had surgeries that involved transplanted dura mater.

Similar to CJD, and an issue with regard to travel, is variant Creutzfeldt-Jacob Disease (vCJD). It also is a rare, degenerative and very similar fatal disorder of the central nervous system, thought to occur after humans have eaten beef contaminated with bovine spongiform encephalopathy (BSE, or “mad cow” disease). In 1996 the first cases of vCJD were reported in the United Kingdom, and there soon was concern on the part of blood banks and public health officials that it could contaminate the blood supply. To date the problem has remained quite rare, with only cases in the United Kingdom (UK) and a few in France and Italy. There has been one case in the United States, but it was in a person who had lived in the UK during the period of greatest risk. So far there have recently been two cases, both in the UK and presumed to have been transmitted via blood transfusion. The USFDA policy seeks to strike a reasonable balance between guarding against the risk of spreading vCJD through blood-banking, and preserving the supply of blood products for medical use. Currently, the policy relates to travel and residence in Europe, and recommends the following individuals be deferred indefinitely:

- those that spent a total of three months or more in the United Kingdom (UK) from the beginning of 1980 through the end of 1996; or who have spent a total of five years or more in Europe from 1980 to the present
- current or former US military personnel, civilian military employees, and their dependents that resided at US military bases in Northern Europe (Germany, UK, Belgium, and the Netherlands) for a total of six months or more from 1980 through 1990; or that resided elsewhere in Europe, such as Greece, Turkey, Spain, Portugal, or Italy, from 1980 through 1996
- those that received any blood or blood component transfusions in the UK between 1980 and the present
- persons that injected bovine insulin since 1980 from cattle raised in the United Kingdom, unless it is possible to confirm the product was not manufactured after 1980 from cattle in the UK.

Guidelines also were issued in 2001 by the US Department of Defense (DoD). They also relate to travel and residence in Europe, and recommend active-duty
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military personnel, civil service employees, and their family members defer indefinitely from giving blood if:

- they traveled or resided in the UK for a cumulative total of three months or more at any time from 1980 through the end of 1996
- they received a blood transfusion in the UK at any time from 1980 to the present
- they traveled to or resided anywhere in Europe for a cumulative total of six months or more at any time from 1980 through the end of 1996; or traveled to or resided anywhere in Europe for a cumulative total of five years or more at any time from 1 January 1997 to the present.

These policies are under constant review by the FDA in light of new information about vCJD and BSE.

There has been much discussion about the development of a test for vCJD that could be used to screen blood donors, but there has been little real progress. In order to be sensitive enough to identify virtually all potentially infectious donations, almost all screening tests will have a false-positive rate. To deal with this it is necessary to have a suitable confirmatory test prior to beginning donor screening. The rationale is that, with the risk of transmission by transfusion being so small, it would be unacceptable to be in a situation of notifying a fair number of volunteer blood donors that they have a test result suggesting they may later develop a fatal disease for which there is no treatment, and when there is uncertainty about the meaning of the test result.

Chagas’ disease

Almost 100 years ago, the Brazilian physician Carlos Chagas discovered the parasite *Trypanosoma cruzi*, which causes Chagas’ disease. Today, it infects as many as 18 million people worldwide. Once established in the body the infection is lifelong, and several thousand South and Central Americans die annually of heart and digestive problems caused by the parasite. Up to 20 percent of infected people never exhibit symptoms. Over the years, Chagas’ disease has often been transmitted by transfusion in South America. Prior to the availability of a test, and since, there has been no treatment for Chagas’ disease. Earlier, gentian violet was added directly to units of blood prior to transfusing them. More recently, testing for Chagas’ disease has become routine in much of South America. While the infection remains rare outside of South and Central America, it has come to be considered a threat to the blood supply because of global travel and migration, especially from South America to North America. To date, there have been only seven cases of transfusion-transmitted Chagas’ disease reported in North America (two of them in Canada), but it is estimated that several million people
from countries where Chagas’ disease is present now reside in the United States, and 100,000 or more may be infected with *T. cruzi* (Kirchoff et al., 1987). In several investigational studies of US blood donors with confirmed sensitive tests, so far there has been only a handful of cases of blood donors with confirmed positive tests, but not all have been tracked to donors from countries where Chagas’ disease is endemic. As a precaution, the American Association of Blood Banks’ guidelines prohibit blood donation from anyone who has had Chagas’ disease. Laboratory and screening tests are now under development. It is expected that, when approved, such testing will be implemented routinely on all donations.

**Babesiosis**

Babesiosis is a parasitic infection of red blood cells caused by the protozoa *Babesia microti*, similar to malaria, and carried by the white-footed mouse and transmitted by deer tick bites. It appears primarily in the northeastern United States, in coastal areas that are home to the white-footed mouse. Cases also have been identified in the Upper Midwest and Pacific Northwest. Approximately 60 transfusion-associated cases have been reported in the United States. While babesiosis often is quite mild, some patients (including those without a spleen, the elderly, or the immunocompromised) may be at risk of serious illness. Occasionally babesiosis is misdiagnosed as malaria, but when correctly diagnosed appropriate antibiotic therapy is effective. There are no useful tests available for screening blood donors, although testing strategies are being discussed. The American Association of Blood Banks (AABB) requires that all donors be asked if they have a history of babesiosis, and individuals with a history of the disease are deferred from donating blood.

**Lyme disease**

The social ecology of Lyme disease is related to the migration of the population in developed nations to suburban areas (see Chapter 5). It is associated with the bite of the same species of deer tick as is the vector for babesiosis, and can cause an illness that affects many systems within the body. Despite a number of researchers looking for examples of Lyme disease transmitted by transfusion, none has been found; and this is probably because it is present in blood and potentially capable of being transmitted by transfusion for only a very short period of time. There is one interesting case of an individual thought to have been positive for both Lyme disease and babesiosis whose blood donation transmitted only babesiosis but not Lyme disease (Cable et al., 1993; McQuiston et al., 2000). While transfusion-related cases have not been reported, public health agencies and the AABB are monitoring this disease because of the remote chance that it could affect transfusion safety. People with a history of Lyme disease can
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give blood provided they have completed a full course of antibiotic treatment and no longer have any symptoms.

Ehrlichiosis

First discovered in 1994, human ehrlichiosis (HE) is a bacterial infection caused by several types of rickettsiae that spread by tick vectors from dogs and other animals to humans. Like Lyme disease, ehrlichiosis is occurring in a context of widening suburban sprawl in North America, Europe, and Japan. Once in the bloodstream, the bacteria invade and kill white blood cells. There are two types of ehrlichiosis: human granulocytic (HGE) and human monocytic ehrlichiosis (HME). The threat to the blood supply appears to be primarily from HGE. From 1986 to 1997, there were only 449 cases of HGE reported in the United States. Symptoms include relatively mild and self-limited fever, headache, and malaise. However, 10–20 percent of people with HGE go on to suffer encephalitis, acute respiratory distress syndrome, and opportunistic infections, and up to 5 percent of infections may be fatal. Treatment with antibiotics such as tetracyclines is effective. The incidence of HGE is not well understood among blood donors, with perhaps only one presumptive case in a blood recipient. Preliminary studies indicate that HGE can survive in refrigerated blood for up to 18 days (Walker and Dumler, 1997; Leiby et al., 2002).

Severe acute respiratory syndrome (SARS)

SARS is a respiratory infection that can produce serious complications. Most cases identified have been in Asia, but there have been outbreaks elsewhere, including the United States and Canada. To date, there has been no evidence of SARS transmission through blood transfusion. However, the potential exists, because the virus associated with SARS is present in the blood of people who are sick. If it were possible for the virus to be present in blood before an individual becomes ill and for that person to donate blood, then that individual potentially could introduce the virus into the blood supply. To prevent this from occurring, blood collection facilities ask potential donors orally or in writing about recent travel to a SARS-affected country, a history of SARS infection, or possible exposure to SARS. Because the risk of contracting SARS through a blood transfusion theoretically exists during periods of SARS epidemics anywhere in the world, anyone who has traveled to a SARS-infected area or who has had close contact with a person with SARS or someone suspected of having SARS is asked to refrain from donating blood for at least 14 days after arriving in the United States. “Close contact” is defined as having cared for, lived with, or had direct contact with the respiratory secretions and/or body fluids of a person known to have, or to have had, SARS. Anyone who has been ill with SARS or...
suspected SARS should refrain from donating blood for 28 days from the last date of treatment and symptoms. In addition, all donors are asked to call the blood center after donating if they then become ill. If this call occurs prior to the blood being transfused, the unit(s) can be intercepted and destroyed. As long as a donor is and remains well, no other measures are necessary.

**Negligence, human error and failed oversight**

In the United States and other developed nations, errors in blood component preparation and testing are nowadays very rare – primarily due to bar-coding of all donor registration forms, blood donations, components, and sample tubes, as well as to large-scale automation of viral testing and testing for blood type, with computerized assimilation of all these test results to each pertinent blood donation. One type of error that can still occur is at the blood collection site, in the labeling of the form, the donation and/or the tubes of collected blood. Below are two examples of how human errors such as this might occur.

1. While each blood donor is handled separately from the others, a staff person evaluating the donor’s history can turn the donor and the form over to another staff person, and then to the venipuncture technician to collect the blood and the tubes for testing. As a check, a second staff person is tasked to ask the donor to provide his name again so it can be checked with the paperwork before collecting the unit. If this check is not performed correctly, one donor’s identifying information can become associated with another donor’s unit of blood. While the donated unit will have all of the test results associated with it, if the donor subsequently calls back (this is an infrequent event) saying that he has developed a fever or has just learned of recent prior exposure to hepatitis, the wrong unit of blood will be recalled, and the one that should be recalled could be transfused.

2. A more ominous error would be a mix-up between the “whole blood number,” with its associated bar code of one unit of blood, with the numbering on the tubes for testing from another donation. The bar code and number are manually placed on each of three or four tubes for testing, and on the unit of blood itself. If a staff person is interrupted during the placing of these bar codes on tubes and bags, or if the wrong tubes are picked up for filling just before or after collection of the unit of blood, then the test results will be associated with the wrong unit for transfusion. If one donor’s test results are positive, the unit could still be labeled as acceptable due to clear test results from the other donor, and transfused. Since 80 percent of blood donations are from repeat donors and the blood type on prior donations is checked before labeling the current donation, the blood center most probably will know an error has occurred, will investigate, and will prevent the labeling and release of all
potentially affected units if the blood types on the two donors are different (e.g. one is A positive and another is O negative). Finding such a discrepancy is a very rare event, due to the emphasis on training collection staff about the importance of donor identity and proper handling of blood samples and unit labeling. In addition, hospitals are required to re-check the ABO and Rh type of each unit of labeled blood they receive from a blood center before issuing it for transfusion to a patient. The consequence of adhering to strict procedures is that finding such a discrepancy at the hospital is a very, very rare event. Nevertheless, the practice of continuing this last check at the hospitals continues. If a test tube or unit does not have a proper number with bar code on it, it is not tested and not used, and the donation is discarded.

A number of high-profile scandals have occurred in blood-banking in developed nations, most notably during the first years of the AIDS epidemic, but also related to hepatitis C. One occurred in Canada, where in 1984 the Canadian Red Cross Society was importing plasma donations from the United States. At the time it was widely known that the AIDS epidemic in the United States had been associated with blood transfusion, especially among people with hemophilia. Meanwhile, Canada was not fully self-sufficient in its supply of blood products and, in particular, did not have adequate supplies of Factor VIII concentrate (the plasma derivative) for people with hemophilia. The Canadian Red Cross was faced with the difficult problem of weighing the risk of importing potentially tainted blood products against that of putting hemophiliacs at risk because of insufficient supplies of clotting agent. The Canadian Red Cross chose to continue importing US supplies. However, while the US Centers of Disease Control had in 1984 approved a test for HIV in blood, the Canadian Red Cross did not implement testing until late 1985.

A national scandal erupted when critics accused the government and the Canadian Red Cross of denial and negligence. In 1988, the Canadian Hemophilia Society requested compensation for victims. They were ignored. The victims persisted. In 1993, the Federal Government appointed a Commission of Inquiry, headed by Justice Horace Krever, to investigate the spread of HIV and hepatitis C through the blood-banking system. They concluded that Red Cross and Government oversight had led to failure to act in a timely manner to prevent the spread of HIV and hepatitis through the blood supply, that the system had been under-funded, and that Canada lacked a strong national blood policy with clear lines of responsibility across organizations and agencies involved in the entire process of blood-banking. Victims and families were awarded compensation. The Commission also concluded that donated blood is a national public resource, and safety is paramount. A national independent board was established, national standards were promulgated, and in 1998 the Red Cross was replaced by the new Canadian Blood Services to manage the blood-banking system. In 2004, federal, provincial, and territorial governments announced the country’s first national
standards to govern the handling of blood and blood products from “vein-to-vein.” In May 2005, the Canadian Red Cross apologized and pleaded guilty to distributing tainted blood products. Dr Roger Perrault, the National Medical Director of the Canadian Red Cross at the time of the scandal, three other physicians, and Armour Pharmaceuticals (located in the United States) were put on trial for criminal negligence. That proceeding continues. It is estimated that perhaps 20,000 people were infected with hepatitis C, and about 1000 with HIV.

As in Canada, epidemics of contaminated Factor VIII concentrate products for hemophiliacs also occurred in France and Japan during the 1980s. Scandals also erupted when it was recognized that high-level government officials either knew or should have known that the products were unsafe, and were culpable for permitting them to remain in use. In France, perhaps 4000 individuals were infected. Three French officials were charged: the former Premier, Laurent Fabius; his superior at the time, the Social Affairs Minister Georgina Dufoix; and the Health Minister responsible for oversight, Edmond Hervé. At the core of the charge of negligence was that the three had delayed introducing the US blood-screening test into France until a rival French product was ready to go on the market. Hervé was convicted of negligence for HIV acquired by two recipients of the products, but the court failed to hand down punishment. Still, at least there was public recognition of official responsibility (BBC News, 1999). In Japan, more than 1400 hemophiliacs were exposed to HIV and at least 500 died as a result. The scandal raised a national outcry about whether the Japanese Government’s health bureaucracy was too tied to the pharmaceutical industry, and thereby put profits over people. Akihito Matsumara, head of the Government Ministry responsible for handling blood and blood products, was charged with negligence and given a suspended one-year sentence for the death of a patient who in 1986 contracted AIDS from a contaminated transfusion. By that time, heat treatment to sterilize blood replacement products from HIV had been in place in the United States for two years (BBC News, 2001).

A much larger epidemic of HIV, hepatitis, and possibly other infectious diseases may have occurred in China as a result of unsafe practices by unscrupulous private blood collection companies too closely linked with government officials. These enterprises operated in Henan, Anhui Shaanxi, and Hebei provinces, where mostly poor rural Chinese were paid to donate blood. They re-used non-sterile blood collection equipment between donors and re-infused repeat donors with potentially tainted blood in order to reduce their symptoms of anemia and get them to donate more often. So far there has never been a full surveillance program to document the extent of the epidemic, but it could be very large, because the combined population of these provinces is about equal to that of Western Europe. Not only are the donors at risk, but also their sexual partners. Activists who protested that there was a Government cover-up were beaten and jailed. In February 2002, proof of official Government participation in the blood donor scheme appeared in the form of a videotape sent to the United Nations,
the PRC Ministry of Health, and the news media. It showed 20 villagers’ blood donor cards that had been issued by the Henan Ministry of Health, and that the individuals had been allowed to be repeat donors. It was not until March 2004, approximately seven years after the beginning of the epidemic, that the national Ministry of Health acknowledged that transmission of HIV had occurred in the 1990s due to blood collection. To date, no individual Chinese official has been held responsible (Agency France Press, 2004; Wan and Li, 2007).

Responding to the challenges ahead

Maintaining a safe blood supply will require constant vigilance on the part of blood-banking and public health officials. No one could have predicted the enormous challenges created by the AIDS pandemic, and no doubt new challenges will arise in the years ahead. One such relatively new concern is terrorism (see Chapter 12). Officials in the United States are concerned about the possibility that terrorists could obtain access to the smallpox virus and use it against the public. Before 1972, vaccinia, the live virus used in smallpox vaccinations, was routinely administered to Americans. Smallpox can be highly infectious – for example, a scab at the inoculation site can contain infectious virus, so it is possible for a scab that spontaneously separates from the skin to inadvertently infect close contacts that touch the vaccination site or dressing. Another area of concern is blood-banking. In response to this potential threat, the United States Department of Health and Human Services (HHS) has been working with state and local governments to strengthen preparedness. Part of the strategy is to expand the national stockpile of smallpox vaccine, which is highly effective when administered shortly after exposure. To make certain the virus is not transmitted through a blood transfusion, potential donors will be asked at blood collection facilities about a history of vaccination or close contact with anyone who has been vaccinated. A vaccine recipient who has had no complications may donate after the vaccination scab has spontaneously separated, or 21 days after vaccination, whichever is the later. Individuals who receive a smallpox vaccination may be asked to refrain from donating for an interval of two months if a scab was pulled off or knocked off (i.e. did not spontaneously separate), and to refrain for 14 symptom-free days if there has been a complication or contact with a vaccine recipient that developed skin lesions or other complications. If smallpox vaccinations were to be administered rapidly to a large section of the population, this would have a substantial negative effect on the blood supply, particularly platelets. The current FDA recommendation is for individuals to refrain from donating blood for one month after smallpox vaccination.

Another future consideration for blood safety is “pathogen inactivation.” Several large corporations have spent hundreds of millions of dollars exploring this. There are different approaches to pathogen inactivation of red cells, platelets,
and plasma; since the functionality of red cells, platelets, and plasma proteins are different in their fragility, the function of each must be preserved to be effective. These approaches involve exposing each single blood component to a chemical, sometimes along with UV light, such that viruses, bacteria, and parasites would be inactivated and no longer infectious. These processes require addition of inactivating chemicals to the blood, then washing out these chemicals so the patient is not exposed to the chemical. To perform this inactivation on each component would be expensive and require very large laboratories, and would generate huge volumes of hazardous waste (the wash solution). Due to the increasing safety of blood for transfusion that has occurred in the last 20 years, it is questioned whether this (now) small incremental (theoretic) improvement in safety is worth the huge expense (and risk to staff in handling all these chemicals). Clinical trials of these processes have been terminated (red cells), though some continue (platelets).

Traditionally a conservative group, blood-bankers, sensitive to patient safety, public perception, and regulatory agencies (e.g. FDA), have been slow to change longstanding processes developed earlier to improve safety. Following this tradition, more and more tests will be added to each donation, more and more questions will be asked of all prospective donors, and more and more donors will be deferred – such that the blood supply will dwindle. To offset this, major initiatives to encourage donations from new donors, and more frequent donations from existing suitable donors, will continue to be needed.

For some time it has been a popular lay belief that “artificial blood” or “synthetic blood” will solve this problem. Truly synthetic blood is represented by perfluorocarbons that can carry and release oxygen. Several trials have been discontinued due to safety concerns. Other problems include that the beneficial effect is brief, administration of 100 percent oxygen is required during its use, and the recipient patient’s blood is then milky, interfering with the interpretation of many clinical laboratory test results. These perfluorocarbons have no role other than oxygen delivery, and cannot supplant the need for platelet or plasma transfusion.

Some refer to stroma-free hemoglobin solutions as artificial blood, but the source is still blood. Advantages include extended shelf-life and more lax storage conditions, no need to match blood type, and presumed lack of infectious risk. Some clinical trials with this have been halted due to safety concerns as well, and the beneficial effect in the recipient is short-lived – again, it is just a bridge until transfusion of traditional red cells becomes available. A bovine-sourced hemoglobin continues to face multiple challenges in getting through regulatory and other hurdles.

There is no artificial substitute for platelets on the horizon. Several isolated plasma proteins have been synthesized (Factor VIII and Factor IX for example), and others can be (albumin) but it wouldn’t be cost-effective. No substitute for gamma globulin is expected, since this requires the panoply of antibodies from >1000 donors to all the things these donors have been exposed to. This changes
as the population is exposed to new infectious and other agents to which they make antibodies.

Multiple attempts to grow blood cells in tissue culture and propagate them have not yet been fruitful.

While pathogen inactivation may help to maintain safety for additional infectious threats, it would be expensive. It might eventually, however, permit more individuals to be eligible as donors, and various approaches to pathogen inactivation appear applicable to red cells, platelets, and plasma.

The bottom line is that for quite some time we will continue to be dependent on altruistic voluntary donations from more and more people, and more and more often. If eligible, please give blood. In the United States you can make an appointment at a site convenient to you by calling 1-800-GIVE LIFE. If not eligible, encourage friends, family and acquaintances that may be eligible to donate.

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