Please see p. 3-4

Committee Report

Procurement and transfusion of human immunodeficiency virus-positive or untested autologous blood units: issues and concerns: a report prepared by the Autologous Transfusion Committee of the American Association of Blood Banks

R. YOMTOVIAN, C. KELLY, A.W. BRACEY, S.K. MCCRANEY, S.W. RENNER, K.R. WILLIAMSON, AND S. ATTAR

AMONG THE MOST difficult, controversial, and emotion-laden dilemmas confronting the practice of preoperative autologous transfusion in the 1990s are those related to infectious disease marker testing of autologous blood units in connection with the possible storage and transfusion of infectious units.[1-5] When autologous blood transfusion emerged from decades of dormancy as a new paradigm of transfusion medicine practice in the 1980s, it was widely endorsed as the safest form of transfusion therapy.[6-11] At that time, the perceived goals of autologous transfusion therapy in improving blood transfusion safety were primarily the prevention of transfusion-associated human immunodeficiency virus (HIV), and secondarily the prevention of other transfusion-transmitted viruses. The possibility that autologous blood donors might themselves harbor viral agents, including HIV, was not generally considered. However, as HIV seroprevalence continues to increase and as the donation of blood for autologous use continues to grow (now accounting for an estimated 5% of blood transfusions[12]), so too does the possibility that the donor of autologous blood will be infected with HIV or another blood-transmissible viral agent.

The collection, storage, and transfusion of virally contaminated blood—and especially of HIV-positive blood for autologous use—raise a series of complex medical, ethical, and legal issues, pitting the needs of an individual patient and the physician's obligation to treat against concerns for accidental harm to an "innocent bystander."[13-15] These issues can be summarized in a series of questions.

1. What, if any, is the medical utility of autologous blood transfusion in HIV-positive patients?
2. Is there an ethical mandate for HIV-positive patients to participate in autologous transfusion programs; alternatively, is there an ethical mandate to exclude "dangerous" units from the blood inventory?
3. What, to the best of our knowledge, is the risk that an HIV-positive autologous unit will accidentally be transfused to an HIV-negative recipient, and how does this risk compare to other life-threatening iatrogenic risks faced by hospitalized patients?
4. Should infectious disease marker testing of autologous blood be mandated?
5. What steps are required to ensure that the recipient receives the correct transfusion unit?
6. Are universal precautions adequate to protect personnel involved in the handling of HIV-positive units?
7. Are there laws and or/legal precedents that affect the participation of HIV-positive patients in autologous donor programs?

The purpose of this article is to explore these complex issues, providing the background requisite to the development of policy on the procurement and transfusion of infectious or untested autologous blood.

What is the Medical Utility of Autologous Blood Transfusion in HIV-positive Patients?

It is imperative, using HIV as a model for any significant infectious marker positivity, to affirm the medical utility of autologous blood transfusion in the treatment of patients, irrespective of their HIV antibody status.

Abbreviations: ADA = Americans with Disabilities Act; BPAC = Blood Products Advisory Committee; FDA = Food and Drug Administration; HIV = human immunodeficiency virus.

From the Institute of Pathology, Case Western Reserve University, and the Department of Pathology, University Hospitals of Cleveland, Cleveland, Ohio; the Department of Government and Legal Affairs, American Association of Blood Banks, Bethesda, Maryland; the Department of Pathology, St. Lukes-Episcopal Hospital, Houston, Texas; American Red Cross Blood Services, South Carolina Region, Columbia, South Carolina; the Laboratory Service, Veterans Administration Medical Center, Los Angeles, California; the Section of Transfusion Medicine, Mayo Foundation, Rochester, Minnesota; and the Department of Thoracic Surgery, University of Maryland Hospital, Baltimore, Maryland.

The views expressed in this article represent the opinion of the authors and are not official policy of the American Association of Blood Banks.

Received for publication October 6, 1994; revision received December 16, 1994, and accepted December 22, 1994.

Clearly, while the development and growth of autologous transfusion practice was catalyzed, initially, by the goal of preventing transmission of transfusion-associated HIV,[16,17] its medical utility goes far beyond this goal. Autologous blood transfusion, as a substitute for allogeneic blood transfusion, is potentially effective in eliminating nearly every risk, known and unknown, associated with allogeneic blood,[18-21] including the transmission of viruses, especially hepatitis and retroviruses; hemolytic transfusion reactions; febrile and allergic reactions; immunization of the recipient to foreign red cell, white cell, and platelet antigens; graft-versus-host disease; and, presumably, posttransfusion immunosuppression. Furthermore, since we cannot predict what new risks, especially new agents of infectious disease, may emerge in the future or when they may emerge, autologous transfusion serves an important preventive role.[22] Nonetheless, reports of the transmission of *Yersinia enterocolitica* by autologous blood transfusion[23,24] serve to underscore the inherent risks associated with transfusion, even of autologous blood.[25]

While there has been a spirited debate regarding the cost-effectiveness of preoperative autologous blood donation,[26-35] particularly in those procedures with minimal likelihood for requiring transfusion support, there is an overwhelming, broad consensus that autologous blood is medically indicated as the safest form of transfusion therapy in scheduled, elective surgical procedures in which the typical blood loss often necessitates blood replacement.[29,36] Even the Health Care Financing Administration, which now considers autologous blood transfusion as a covered service,[37] does so under the caveat that covered services by definition are those that are medically reasonable and necessary. Section 1862(a)(1)(A) of the Social Security Act provides that the Medicare program may not pay for items or services that are not "reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."[38]

It is possible that specific immunocompromised HIV-positive transfusion recipients are at particular risk for adverse effects of allogeneic blood transfusion. Secondary viral infections are often more severe in HIV-positive persons.[39-44] In addition, secondary viral infections may enhance HIV replication and accelerate the clinical course.[39,42,45-51] Finally, allogeneic blood itself—possibly either white cells and/or plasma alloantigens from HLA-mismatched blood—may lead to transfusion-associated immunosuppression and virus activation in HIV-positive persons.[52,53] Indeed, it has been suggested that the receipt of blood components during the course of HIV infection is associated with more rapid disease progression.[54,55] While it is possible that white cell reduction in blood will ameliorate this effect (a federally funded clinical trial is underway to assess this), it is premature to equate white cell-reduced blood with autologous blood. Thus, as the survival period of HIV-infected individuals increases,[56] autologous blood may actually be of equal or greater benefit to HIV-positive persons than to HIV-negative persons.[57]

Is There an Ethical Mandate for HIV-positive Patients to Participate in Autologous Blood Transfusion Programs?

In 1988, the Council on Ethical and Judicial Affairs of the American Medical Association and the Health and Public Policy Committee of the American College of Physicians and the Infectious Diseases Society of America issued documents offering ethical guidance for physicians in caring for HIV-infected patients.[58,59] These groups strongly emphasized the need to avoid discrimination in the care of patients who are HIV seropositive. They affirmed that a physician may not ethically deny medical care to a patient solely on the basis of HIV seropositivity. In 1991 and 1993, the Council on Ethical and Judicial Affairs reaffirmed the physician's ethical responsibility to care for HIV-positive patients,[60,61] stating in part, "Any discrimination that emanates from members of the medical profession is particularly objectionable because of medicine's professed commitment to moral ideals.... Nor can physicians expect less medically sophisticated members of the public or government officials to react to health crises with reason and compassion when they themselves do not demonstrate these characteristics."[60(p2876)] Most recently, the Health and Public Policy Committee of the American College of Physicians and the Infectious Diseases Society of America reinforced their previous stance by maintaining that "[t]he denial of appropriate care to a class of patients for any reason is unethical."[62(p312)]

Under this ethical mandate, since autologous transfusion is a medical service provided to patients on a case-by-case basis, HIV serostatus in and of itself is likely insufficient to exclude HIV-positive or untested persons from autologous blood donation. Indeed, the Food and Drug Administration (FDA) currently allows, but does not recommend, the use of autologous units that test positive (provided they are appropriately labeled as a biohazard and provided that the attending physician specifically requests their use in writing).[63,64] In struggling to maintain the rights of patients, however, blood bank professionals are confronted with a difficult ethical dilemma. Should the medical treatment of HIV-infected patients, in the form of autologous transfusion therapy, be set aside to avoid the possible risk of accidental injury? The answer rests with our confidence in the integrity of our operating systems to effectively minimize errors and with our commitment to the ethical mandate to provide medical treatment to all individuals regardless of HIV serostatus.

What is the Risk that an HIV-positive Autologous Unit Will Accidentally be Transfused to an HIV-negative Recipient?

The risk of accidental transfusion of an HIV-positive autologous unit to an HIV-negative recipient is unknown. There have been no documented instances. Furthermore, the risk of this occurrence is likely to vary from institution to institution according to the integrity and reliability of the systems used to detect and prevent errors. As discussed by Dzik and Devarajan[65] in a decision analysis approach to infectious marker testing of autologous blood, where errors are common, the medical utility to an individual patient, no matter how great, will be offset by the greater risk of harm to an "innocent bystander."

In a study by Renner et al.[66] evaluating wristband identification errors in 712 hospitals participating in a College of American Pathologists study of quality issues in transfusion practice, wide variation in the error rate was noted from institution to institution. Thus, whereas the mean error rate was 5.5 percent, 10 percent of participants reported an error rate of 10 percent or higher (with 5% of institutions reporting error rates of 15% or greater) and 25 percent of participants had error rates of less than 1 percent. According to the available data on 104 transfusion errors reported in the State of New York over the 22 months from January 1990 through October 1991, the risk of inadvertent transfusion of red cells to other than the proper or intended recipient was 1 in 12,000.[67] During the study period, one large institution reported three errors, while most reported none. This study does not isolate data specific to the use of autologous blood.

In a study by Simpson et al.[68] of 175 orthopedic surgery patients receiving autologous blood, there were 12 instances of clerical error, with that factor as the sole source of exposure to allogeneic blood in 2 percent of cases. However, in no instance was autologous blood issued to the wrong recipient. A College of American Pathologists Comprehensive Transfusion Medicine Survey found that, in 20 of 3872 institutions, a unit of autologous blood was reported as being transfused to the wrong patient.[69] Shulman calculated the risk of transfusing a unit of autologous blood to the wrong patient as 1 in 25,000.[70] Analysis of recent data compiled by Linden for New York State estimates this risk at 1 in 16,000.[71] There is a clear need for more comprehensive data on the incidence of accidents and errors involving autologous blood.

The risk of both the random drawing of an HIV-positive unit for autologous use and the subsequent transfusion of that unit to the wrong recipient would be the product of the independent risk of transfusion to the wrong person (on average, estimated at 1/12,000 to 1/25,000, but certainly variable from institution to institution) and the approximate rate of HIV seroprevalence in autologous units. Analysis of recent data compiled from all American Red Cross Blood Service Regions between April 1993 and March 1994 demonstrated, on a unit-by-unit basis, that the HIV positivity rate for autologous blood donations was 1 in 10,000, as compared to 1 in 25,000 for allogeneic blood donations.[72] Although HIV seroprevalance on a unit-by-unit basis is higher for autologous blood than for allogeneic blood, there still is only a 1 in 120,000,000 to 1 in 250,000,000 chance of the random, accidental transfusion of an HIV-positive autologous unit to an HIV-negative recipient. This risk should be compared to the reported 1 in 600,000 chance of fatality secondary to receipt of an ABO-incompatible blood transfusion.[67]

In addition, it is of interest to compare the level of transfusion-associated risks with the occurrence of adverse events and accidental injury catalogued, overall, for hospitalized patients. The Harvard Medical Practice Study[73,74] quantitated adverse events documented in 30,121 randomly selected patient records from 51 hospitals in New York State in 1984. Adverse events were identified in 3.7 percent of hospitalizations. The authors, extrapolating this to all discharges in New York in 1984, calculated 2,671,863 discharges and 98,609 adverse events. Adverse events were classified as unavoidable—related to medical management and not due to substandard care (non-negligent)—and avoidable—related to substandard care (negligent). Of total adverse events, 28 percent (27,179) were associated with negligence. Of total discharges, 1 in 388 (6,895/2,671,863) was associated with death due to negligence. Under the tort system, the authors felt that all of these cases could have been successfully litigated. Although the Harvard Study documented no specific instance of transfusion associated fatality, according to the definition provided above, the accidental transfusion of an ABO-incompatible unit or of an HIV-positive autologous unit to someone other than the intended recipient would be classified as negligence. Thus, the estimated risk of death due to overall negligence, as noted in the Harvard Study, is more than 1500 times greater than the risk of death due to a negligent ABO-incompatible transfusion and more than 300,000 times greater than the hypothetical risk of death due to negligent receipt of an HIV-positive autologous unit.

It is evident that hospitalization places the patient at substantial risk for an adverse event, including death. While significant risks associated with negligence in blood transfusion appear to be comparatively small, potentially avoidable accidents continue to occur. Reductions in the occurrence of accidents and error will depend primarily on a thorough analysis of our systems and the development, whenever possible, of fail-safe systems that make it virtually impossible ("as low as reasonably achievable," or ALARA[75]) to order blood for or dispense blood to the wrong patient. As the Harvard Medical Practice Study authors noted, "Adverse events result from the

interaction of the patient, the patient's disease, and a complicated, highly technical system of medical care provided not only by a diverse group of doctors, other care givers, and support personnel, but also by a medical-industrial system that supplies drugs and equipment. Reducing the risk of adverse events requires an examination of all these factors as well as of their relation with each other."[74(pp383-4)] This is a difficult but worthwhile challenge, one that blood bankers have traditionally embraced. Failure to succeed in this endeavor means that patients are placed at risk not only for the possible inadvertent transfusion of an HIV-positive autologous blood unit but, more important, that patients will be placed at risk for the recurrent possibility of an ABO-incompatible blood transfusion.

A recent report from Belgium describes 7 allogeneic red cell transfusions, out of 2772 over a 15-month period, administered to incorrect recipients through errors thought to have occurred after the blood had left the blood bank.[76] These were identified by review of records within 5 working days of the transfusion. In only one instance (a small amount of group B blood given to a group O recipient) was a reaction noted. However, in no instance was the discrepancy actually recognized and reported to the blood bank. While more stringent policies for identification prior to blood transfusion are thought to be in place in the United States, should the data in this study prove verifiable by concurrent analysis and therefore be generalizable, the risk of transfusion of an allogeneic unit to an incorrect patient would be approximately 1 in 400 rather than the currently assumed estimate of 1 in 12,000. Such a presumed "bedside" error rate underscores the urgent need for all steps in the blood transfusion process, including those steps that follow the blood's departure from the blood bank, to be held to the same rigorous standards.[77]

Should Infectious Disease Marker Testing of Autologous Blood be Mandated?

As autologous transfusion practice became increasingly popular in the late 1980s, many institutions, especially blood centers, used the same donor history questions and laboratory screening tests for allogeneic and autologous blood donors. Because of the high rate of wastage of autologous blood, it was felt that this would allow improved utilization if nontransfused autologous units that met the same rigid standards as allogeneic blood could be crossed over for routine allogeneic use.[78] In the ensuing years, however, crossover activity has greatly diminished, with only about 30 percent of autologous blood eligible by allogeneic criteria to be given to other recipients[79] and only an estimated 2 percent of units actually crossed over.[80] With interest in crossover waning,[5] some facilities have streamlined the autologous blood donor history and unit labeling procedures. Donor questioning now focuses only on direct health risks to the donor. A natural extension of this process would be the complete elimination of infectious marker testing of autologous units. In accordance with current, applicable FDA guidelines, the procurement, storage, and transfusion of autologous units that are not tested for markers of infectious disease have already been safely performed for many years at numerous hospital facilities that collect autologous blood units as well as transfuse them.[33]

It was further argued, intuitively, that adherence to an identical standard operating procedure, while not needed for autologous blood, would reduce the likelihood of error. Indeed, from the viewpoint of administrative simplicity and standardization, it may be argued that units of autologous and allogeneic blood should be handled identically, with testing of all units and discarding of all units with confirmed positive test results.[5,81] In this regard, the British Committee for Standards in Haematology Blood Transfusion Task Force recently issued guidelines for preoperative autologous blood donation.[82] In the section "Practical aspects of collection, storage and transfusion," the task force advises that, as a minimum, on the first and last autologous donations in a series, tests for hepatitis B surface antigen, antibodies to HIV types 1 and 2, and antibodies to hepatitis C virus be performed to "establish the patient's status for these markers and because current practices are such that donations which are positive for any of these tests would not be issued for use and the same criteria should apply for autologous transfusion.... [A]ny donation(s) which have been collected should be discarded with appropriate precautions and the autologous programme for the patient should be abandoned."[82(pp309-10)] A loophole is provided, however, in that, as stated in the introduction, "[I]t is recognized that exceptional circumstances may arise and that the final decision regarding the use of autologous pre-deposit rests with the doctor who undertakes the procedure."[82(p307)] This policy is noted to be in compliance with current Guidelines for the Blood Transfusion Services in the UK as set forth by the UK Department of Health in 1993.

Most recently, at the invitation of the FDA, the FDA Blood Products Advisory Committee (BPAC) met on June 21, 1994, and recommended to the FDA that autologous blood and blood components be tested for all infectious disease markers for which allogeneic blood and blood components are tested.[72] However, collection facilities would be given the option of testing only the first unit of blood collected from a donor in a 30-day period. The BPAC further recommended that blood and blood components not be used for autologous transfusion if screening tests are repeatedly reactive and additional, more specific tests are not negative. However, as is consistent with current policy, the use of infectious disease marker-

positive units would be permitted after a written, signed, and dated authorization was received from the clinician.[72]

These strategies of routine infectious marker testing and recommended discarding of marker-positive units raise a number of important issues. 1) Each strategy may result in the discarding of noninfectious units with positive screening tests if confirmatory test results are available after the need for the autologous blood has passed or if indeterminate results are obtained. Thus, autologous units of individuals who really do not have a transmissible disease could be denied them if the screening tests are done. 2) The BPAC recommendations, in contrast to the British guidelines, apparently would apply to rapid plasma reagin- and/or fluorescent treponemal antigen-positive units, which would lead to the possible discard of these "low-risk" units. 3) The BPAC recommendations, in contrast to the British guidelines, might mean that autologous units will in many instances be tested for alanine aminotransferase. Although the FDA does not require or recommend alanine aminotransferase testing, it is possible that many facilities, under the BPAC recommendations to test allogeneic and autologous units by identical required tests, will exclude potential donors on the basis of elevated alanine aminotransferase. 4) Each strategy adds a layer of administrative complexity and confusion that is particularly evident when discarding is recommended but not mandatory. A clinician may desire to transfuse, but the transfusion facility may refuse to receive, HIV- or other marker-positive autologous blood; surgery will at times be canceled or delayed; and inadvertent transfusion to the wrong individual will still be possible since infectious disease marker-positive units may be maintained in the inventory. 5) Each strategy adds a significant cost burden to the already costly autologous blood system,[26,81] and this has been identified as an important impediment to optimal use.[29] 6) Each strategy serves to deny the application of autologous transfusion to a group of patients, already harboring a viral agent, who may be particularly vulnerable to the risks of allogenic blood. 7) Each strategy fails to address the most common cause of accidental transfusion-associated fatalities, namely, the inadvertent transfusion of an ABO-incompatible unit.[84] 8) Each strategy fails to significantly reduce the incidence of posttransfusion HIV infection via tested units, an incidence estimated at 1 per 225,000 transfused units,[85] which is overwhelmingly a result of limitations in the donor screening process and not of transfusion error.

Rather than focusing only on the testing of autologous blood as a hypothetical yet costly strategy for improving transfusion safety, we should be investigating a more global strategy encompassing the development of mechanisms designed to effect systemwide error reduction, including those mechanisms relating to the accidental transfusion of ABO-incompatible blood and potentially marker-positive autologous blood. Such an approach would be similar to that recently recommended for dealing with HIV-positive surgeons: "If we want to reduce the risk of HIV transmission, resources are spent more effectively on education and infection control, including the development of improved methods and compliance, than on locating and avoiding or removing infected surgeons."[86(p1370)]

What Steps are Required to Ensure That the Recipient Receives the Correct Transfusion Unit, Whether Allogeneic or Autologous?

Spurred on by public anxiety and the political reaction in the aftermath of the AIDS epidemic, blood banks and transfusion medicine services are under intense pressure to minimize accidents and errors. This pressure has prompted the FDA to place a renewed emphasis on quality. In addition to Current Good Manufacturing Practices for blood and blood components, the FDA now mandates the application of Pharmaceutical Current Good Manufacturing Practices.[77] The essence of Current Good Manufacturing Practices is the assurance of the safety and effectiveness of blood.

The goal is not merely to detect errors, but to engineer systems and processes to prevent errors.[87,88] Possible approaches to error prevention include the use of an institutionally validated system designed to ensure the identification of the autologous donor-patient from unit procurement to transfusion; the development of computer programs to track the autologous unit from collection to transfusion and to impede the release of incorrect blood units; the prohibition of simultaneous release of autologous and allogeneic blood to an individual patient; the elimination of crossover of autologous blood to use as allogeneic blood; the development of a standardized identification system for collection and transfusion facilities to reduce the likelihood of errors during shipping; the use of a physical barrier system (e.g., Blood-Loc, Novatek Medical, Greenwich, CT) to hinder transfusion of an incorrect unit[89,90]; the development of a blood bank-based transfusion team to coordinate all aspects of transfusion from specimen procurement to component transfusion[91]; the strict application of FDA and American Association of Blood Banks regulations and standards to transfusion-associated activities occurring not only inside but also outside of the jurisdiction of the blood bank, coupled with ongoing education; the verification of those who control any aspect of the transfusion process as responsible and accountable for the outcome; and the use of ongoing audits.[92,93]

The possibility that a rare unit of autologous or even allogeneic blood within our inventory may harbor HIV or another blood-transmissible virus should be reason enough for consideration of ways to ensure that the in-

tegrity of the transfusion loop is unbroken and the risk of error is as low as reasonably achievable. In this way, it should be possible "to protect and promote both the public health and individual rights."[94(p45)]

Are Universal Precautions Adequate to Protect Personnel Involved in the Handling of HIV-positive Units?

Universal precautions, the practice of handling blood and body fluids from all patients as though infected with blood-borne pathogens, were introduced by the Centers for Disease Control in 1987[95] and updated in 1988,[96] primarily to help reduce occupationally acquired HIV and hepatitis B virus infections. This practice has been further augmented by the Occupational Safety and Health Administration.[97] While universal precautions are mandated in all instances of anticipated exposure to blood, the extent of protection required depends on the nature of the anticipated exposure. Thus, the Occupational Safety and Health Administration has stipulated that, in a volunteer blood donation center, "routine gloving for all phlebotomies is not necessary," except when the phlebotomist 1) is in training or 2) has breaks in the skin, or 3) when there is judged to be a risk of hand contamination, as for example, with an uncooperative patient. Naturally, gloving would be required when the phlebotomist is drawing blood from patients, such as for autologous or therapeutic donations.[98]

Paradoxically, the requirement for gloving for autologous but not allogeneic donors may mean that autologous phlebotomy, particularly in first-time donors, is less risky than allogeneic phlebotomy, since 1) HIV seropositivity is higher for first-time than for repeat allogeneic donors[99,100]; 2) HIV serostatus for first-time donors will not be known at the time of phlebotomy; and 3) gloves, though they do not reduce the likelihood of a needlestick,[101,102] have been shown to reduce the volume of blood transferred during a accidental needlestick.[103]

In any case, needlestick injuries in blood collection staffers are reported to be rare, estimated in one study at 1 injury per 6000 collections.[104] This, coupled with the approximate HIV seroprevalence in autologous blood units of 1 in 10,000 and the estimated 0.5-percent risk of seroconversion following a needlestick injury, means that a worker's risk of occupationally acquiring HIV during phlebotomy of blood for autologous use is calculated at 12×10^{9}.

Are There Laws and/or Legal Precedents That Affect the Participation of HIV-positive Patients in Autologous Donor Programs?

There are no legal precedents that clearly define the liability ramifications of a policy either to provide or refuse autologous blood services to HIV-positive patients. An institution is likely to encounter litigation whether it provides such services or chooses not to do so.

Under a blanket policy denying autologous blood services to HIV-infected individuals, such patients could make claims under the Americans with Disabilities Act (ADA).[105] The ADA, effective in 1992, required affirmative action to remove barriers that keep disabled people from public accommodations and services.[106] Because a policy denying autologous blood services to HIV-positive patients is, on its face, a denial of a service on the basis of disability, claims under the ADA should be expected if such a policy is adopted.

Under regulations that implement the ADA, on the other hand, a public accommodation is not required to permit an individual to benefit from its services if the individual poses a direct threat to the health or safety of others.[107] A "direct threat" is a "significant risk to the health or safety of others that cannot be eliminated by a modification of policies, practices, or procedures, or by the provision of auxiliary aids or services."[107 §36.208(b)] In assessing whether an individual poses a direct threat, a public accommodation must make an individualized evaluation, on the basis of reasonable judgment that relies on current medical knowledge or on the best available objective evidence, to ascertain the nature, duration, and severity of the risk; the probability that the potential risk will actually occur; and the possibility that reasonable modifications of policies, practices, or procedures will mitigate the risk.[107 §36.208(c)]

Because there is no cure for AIDS, the duration and the severity of the risk of transmission are great. However, to defend a policy denying autologous blood services to HIV-positive patients on the basis of the "direct threat" exemption, consensus should be reached on the probability of virus transmission to HIV-negative patients and health care workers and on the possibility that *reasonable* modifications of existing policies, practices, and procedures can mitigate the risk of mix-ups. Such a consensus position should be supported by documentation in the medical literature, and blood service providers should be prepared to refute studies that take an opposing view.

Because the ADA is relatively new, there is almost no case law on its application. The strength of a direct-threat defense is therefore difficult to assess. Cases adjudicated under the Rehabilitation Act of 1973[108] provide persuasive authority. Court decisions indicate that the level of risk is a key factor in determining whether a violation of the ADA has occurred.[109] (See also *Doe v. Washington University*, 780 F Supp 628 [E.D. Mo. 1991] [challenge of dental student disenrolled by University, rejected by court, which concluded that plaintiff was not "otherwise qualified" because he posed "low but existent risk" of transmission].)

HIV-positive patients would therefore have a fair chance of succeeding in their legal claims of violation of these laws. An individual who files a private action under the ADA is generally limited to injunctive relief, that is, a court could seek an order to change the policy. Under the Rehabilitation Act, and when an ADA suit is brought by the Attorney General, a court could approve compensatory damages. Actual damage to such a patient would seem to be difficult to prove; however, experience shows that juries can be unpredictable when dealing with people with AIDS.

If autologous blood services are provided to HIV-positive patients, an institution may be vulnerable to malpractice claims brought by innocent victims of mix-ups. Monetary damage awards in a successful case could be significant, but an institution might avoid liability if it could show that it adopted and implemented safety precautions to prevent mix-ups and that those measures were comparable to those taken by typical blood banks.

In most states, negligence actions brought by health care workers against their employers are preempted under Worker's Compensation statutes. Moreover, as long as blood service providers inform their health care workers of the risks of working with HIV-positive patients and have procedures in place to protect workers from accidental transmission, any health care worker who brought a negligence claim would have difficulty establishing that the institution violated its duty of care to its employees.

Conclusions

Ultimately, the development of a consensus policy on the use of HIV-positive or untested autologous blood units depends on the interplay of the medical utility of such blood and the public health implications of an accident or error resulting in inadvertent transmission of virus to an innocent party. Further complicating this equation are the attendant legal, ethical, and social concerns. Since data bearing on each of these areas are incomplete and still evolving, and because the risk of accident or error varies greatly from facility to facility, a uniform national policy has not yet been promulgated. Any decisions regarding the use of marker-positive or untested autologous blood should be based on carefully developed and deployed standard operating procedures in each facility, designed to achieve compliance with FDA regulations and American Association of Blood Banks' standards while accommodating, as much as possible, institutional and local practice considerations.

References

1. Mintz PD. Participation of HIV-infected patients in autologous blood programs. JAMA 1993;269:2892-4.
2. Popovsky MA, Hoff RG. HIV-infected patients participating in autologous blood programs (letter). JAMA 1993;270:2181-2.
3. Petz LD, Kleinman S. HIV-infected patients participating in autologous blood programs (letter). JAMA 1993;270:2181.
4. Mintz PD. HIV-infected patients participating in autologous blood programs (reply to letter). JAMA 1993;270:2182.
5. Silvergleid AJ. Preoperative autologous donation: what have we learned? (editorial). Transfusion 1991;31:99-101.
6. American Association of Blood Banks, American Red Cross, and Council of Community Blood Centers, Joint Statement, January 13, 1983.
7. Prevention of acquired immune deficiency syndrome (AIDS): report of inter-agency recommendations. MMWR Morb Mortal Wkly Rep 1983;32:101-4
8. Blood policy and technology. Office of Technology Assessment, Congress of the United States. OTA-H-260. Washington: Government Printing Office, 1985.
9. Autologous blood transfusions. JAMA 1986;256:2378-80.
10. Report submitted to the President of the United States by James D. Watkins, Superintendent of Documents, and Chairman, Presidential Commission on the Human Immunodeficiency Virus Epidemic. Washington: Presidential Commission on the Human Immunodeficiency Virus Epidemic, 1988.
11. National Blood Resource Education Program Expert Panel, National Heart, Lung, and Blood Institute. The use of autologous blood. JAMA 1990;263:414-7.
12. Wallace EL, Surgenor DM, Hao HS, An J, Chapman RH, Churchill WH. Collection and transfusion of blood and blood components in the United States, 1989. Transfusion 1993;33:139-44.
13. Zuger A, Miles SH. Physicians, AIDS, and occupational risk. Historic traditions and ethical obligations. JAMA 1987;258:1924-8.
14. Pellegrino ED. Altruism, self-interest, and medical ethics (editorial). JAMA 1987;258:1939-40.
15. Dan BB. Patients without physicians: the new risk of AIDS (editorial). JAMA 1987;258:1940.
16. Chambers LA, Kruskall MS. Preoperative autologous blood donation. Transfus Med Rev 1990;4:35-46.
17. Sandler SG. Overview. In: Sandler SG, Silvergleid AJ, eds. Autologous transfusion. Arlington: American Association of Blood Banks, 1983:1-9.
18. American Association of Blood Banks, American Red Cross, Council of Community Blood Centers. Circular of Information for the Use of Human Blood and Blood Components, 1994 (revised periodically).
19. Thurer RL, Hauer JM. Autotransfusion and blood conservation. Curr Probl Surg 1982;19:97-156.
20. Williamson KR, Taswell HF. Avoiding the hazards of homologous blood transfusion, and other advantages of autologous blood transfusion and hemotherapy. In: Taswell HF, Pineda AA, eds. Autologous transfusion and hemotherapy. Boston: Blackwell,1991:22-52
21. Murphy WG. Adverse effects and complications of transfusion. In: Rock G, Seghachian MJ, eds. Quality assurance in transfusion medicine, vol 2. Boca Raton, CRC Press, 1992:443-69.
22. Lederberg J, Shope RE, Oaks SC Jr, eds. Emerging infections—microbial threats to health in the United States. Washington: Institute of Medicine, National Academy Press, 1992:32.
23. Sire JM, Michelet C, Mesnard R, et al. Septic shock due to *Yersinia enterocolitica* after autologous transfusion (letter). Clin Infect Dis 1993;17:954-5.
24. Richards C, Kolins J, Trindade CD. Autologous transfusion-transmitted *Yersinia enterocolitica* (letter). JAMA 1992;268:154.
25. Linden JV, Kaplan HS. Transfusion errors: causes and effects. Transfus Med Rev 1994;8:169-83.
26. Birkmeyer JD, Goodnough LT, AuBuchon JP, Noordsij PG, Littenberg B. The cost-effectiveness of preoperative autologous blood donation for total hip and knee replacement. Transfusion 1993;33:544-51.
27. Bove JR. Too much of a good thing? (editorial) Transfusion 1993;33:542.
28. Birkmeyer JD, AuBuchon JP, Littenberg B, et al. Cost-effectiveness of preoperative autologous donation in coronary artery bypass grafting. Ann Thorac Surg 1994;57:161-8, discussion 168-9.

29. McCullough J. The nation's changing blood supply system. JAMA 1993;269:2239-45.
30. Etchason J, Calhoun L, Petz LD, Snider C, Fink A, Kleinman S. Cost effectiveness analysis of a predeposited autologous donation (PAD) program (abstract). Blood 1993;82(Suppl 1):394a.
31. Blumberg N, Kirkley S, Panzer R, Heal J. A cost analysis of autologous transfusions in hip replacement surgery (abstract). Blood 1993;82(Suppl 1):587a.
32. Healy JC, Frankforter SA, Graves BK, Reddy RL, Beck JR. Preoperative autologous blood donation in total-hip arthroplasty. A cost-effectiveness analysis. Arch Pathol Lab Med 1994;118:465-70.
33. Kruskall MS, Yomtovian R, Dzik WH, Friedman KD, Umlas J. On improving the cost-effectiveness of autologous transfusion practices. Transfusion 1994;34:259-64.
34. Goldfinger D, Haimowitz M. Controversies in transfusion medicine: Is autologous blood transfusion worth the cost? Pro. Transfusion 1994;34:75-8.
35. AuBuchon JP, Birkmeyer JD. Controversies in transfusion medicine: Is autologous blood transfusion worth the cost? Con. Transfusion 1994;34:79-83.
36. Resolution no. 117: Autologous transfusions for elective surgery. American Medical Association, Proceedings of the House of Delegates, Forty-second interim meeting, Dallas, Texas, Dec. 4-7, 1988. Chicago: American Medical Association, 1988:278.
37. Yomtovian R, Kruskall MS, Barber JP. Autologous blood transfusion: the reimbursement dilemma. J Bone Joint Surg [Am] 1992;74:1265-72.
38. Social Security Act §1862(a)(1)(A); see at 42 U.S.C. 1395y-(a)(1)(A).
39. Eyster ME, Diamondstone LS, Lien JM, Ehmann WC, Quan S, Goedert JJ. Natural history of hepatitis C virus infection in multitransfused hemophiliacs: effect of coinfection with human immunodeficiency virus. J Acquir Immune Defic Syndr 1993;6:602-10.
40. Skolnik P, Kosloff BR, Hirsch MS. Bidirectional interactions between human immunodeficiency virus type 1 and cytomegalovirus. J Infect Dis 1988;157:508-14.
41. Lefrere JJ, Mariotti M, Thauvin M. B19 parvovirus DNA in solvent/detergent-treated anti-haemophilia concentrates. Lancet 1994;343:211-2.
42. Naides SJ, Howard EJ, Swack NS, True CA, Stapleton JT. Parvovirus B19 infection in human immunodeficiency virus type 1-infected persons failing or intolerant to zidovudine therapy. J Infect Dis 1993;168:101-5.
43. Schattner N, Hanuka B, Sarov B, Sarov I, Handzel Z, Bentwich Z. Sequential serological studies of homosexual men with and without HIV infection. Epstein-Barr virus activation preceding and following HIV seroconversion. Clin Exp Immunol 1991;85:209-13.
44. Eyster EM, Fried MW, Di Bisceglie AM, Goedert JJ. Increasing hepatitis C virus RNA levels in hemophiliacs: relationship to human immunodeficiency virus infection and liver disease. Blood 1994;84:1020-3.
45. Greene WC. The molecular biology of human immunodeficiency virus type I infection. N Engl J Med 1991;324:308-17.
46. Rosenberg ZF, Fauci AS. Activation of latent HIV infection. J NIH Res 1990;2:41-5.
47. Schechter M, Harrison LH, Halsey NA, et al. Coinfection with human T-cell lymphotropic virus type I and HIV in Brazil. JAMA 1994;271:353-7.
48. Webster A. Cytomegalovirus as a possible cofactor in HIV disease progression. J Acquir Immune Defic Syndr 1991;4(Suppl 1):S47-S52.
49. Eskild A, Magnus P, Petersen G, et al. Hepatitis B antibodies in HIV-infected homosexual men are associated with more rapid progression to AIDS. AIDS 1992;6:571-4.
50. Knox KK, Carrigan DR. Disseminated active HHV-6 infections in patients with AIDS. Lancet 1994;343:577-8.
51. Lusso P, Gallo RC. Human herpesvirus 6 in AIDS (editorial). Lancet 1994;343:555-6.
52. Busch MP, Lee TH, Heitman J. Allogeneic leucocytes but not therapeutic blood elements induce reactivation and dissemination of latent human immunodeficiency virus type 1 infection: implications for transfusion support of infected patients. Blood 1992;80:2128-35.
53. Blumberg N, Heal JM. Evidence for plasma-mediated immunomodulation—transfusions of plasma-rich blood components are associated with a greater risk of acquired immunodeficiency syndrome than transfusions of red blood cells alone. Transplant Proc 1988;20:1138-42.
54. Vamvakas E, Kaplan HS. Early transfusion and length of survival in acquired immune deficiency syndrome: experience with a population receiving medical care at a public hospital. Transfusion 1993;33:111-8.
55. Sloand E, Kumar P, Klein HG, Merritt S, Sacher R. Transfusion of blood components to persons infected with human immunodeficiency virus type 1: relationship to opportunistic infection. Transfusion 1994;34:48-53.
56. Graham NM, Zeger SL, Park LP, et al. The effects on survival of early treatment of human immunodeficiency virus infection. N Engl J Med 1992;326:1037-42.
57. Balfour HH. Transfusion and human immunodeficiency virus (editorial). Transfusion 1993;33:101-2.
58. Ethical issues involved in the growing AIDS crisis. Council on Ethical and Judicial Affairs. JAMA 1988;259:1360-1.
59. The acquired immunodeficiency syndrome (AIDS) and infection with the human immunodeficiency virus (HIV). Health and Public Policy Committee, American College of Physicians, and the Infectious Diseases Society of America. Ann Intern Med 1988;108:460-9.
60. Clarke OW, Conley RB. The duty to "attend upon the sick." JAMA 1991;266:2876-7.
61. American Medical Association. Digest of HIV/AIDS policy. Chicago: American Medical Association, 1993.
62. Human immunodeficiency virus (HIV) infection. American College of Physicians and Infectious Diseases Society of America. Ann Intern Med 1994;120:310-9.
63. Parkman PD. Guidance for autologous blood and blood components. Rockville: Food and Drug Administration, March 15, 1989.
64. Parkman PD. Autologous blood collection and processing procedures. Rockville: Food and Drug Administration, February 12, 1990.
65. Dzik WH, Devarajan S. Should autologous blood that tests positive for infectious diseases be used or discarded? A decision analysis approach. Transfusion 1989;29:743-5.
66. Renner SW, Howanitz PJ, Bachner P. Wristband identification error reporting in 712 hospitals. A College of American Pathologists' Q-Probes study of quality issues in transfusion practice. Arch Pathol Lab Med 1993;117:573-7.
67. Linden JV, Paul B, Dressler KP. A report of 104 transfusion errors in New York State. Transfusion 1992;32:601-6.
68. Simpson MB, Georgopoulos G, Orsini E, Eilert RE. Autologous transfusions for orthopedic procedures at a children's hospital. J Bone Joint Surg [Am] 1992;74:652-8.
69. Comprehensive transfusion medicine survey, set J-C. Northfield, IL: College of American Pathologists, 1992.
70. Shulman I. Your worst transfusion nightmares. Presented at an American Society of Clinical Pathologists workshop, Orlando, FL, Oct. 16, 1993.
71. Linden J. Autologous blood errors and incidents (abstract). Transfusion 1994;34(Suppl):28S.
72. Blood Products Advisory Committee, Center for Biologics Evaluation and Research, Food and Drug Administration, Public Health Service, Department of Health and Human Services. Meeting Transcript, 44th meeting, June 21, 1994:68-159. Available by writing to: Freedom of Information Office, HFI-35, Food and Drug Administration, 5600 Fishers Lane, Room 12A-16, Rockville, MD 20857.
73. Brennan TA, Leape LL, Laird NM, et al. Incidence of adverse events and negligence in hospitalized patients: results of the Harvard Medical Practice Study I. N Engl J Med 1991;324:370-6.

74. Leape LL, Brennan TA, Laird N, et al. The nature of adverse events in hospitalized patients. Results of the Harvard Medical Practice Study II. N Engl J Med 1991;324:377-84.
75. Zuck TF. Greetings—a final look back with comments about a policy of a zero-risk blood supply (editorial). Transfusion 1987;27:447-8.
76. Baele PL, De Bruyere M, Deneys V, et al. Bedside transfusion errors. A prospective survey by the Belgium SAnGUIS group. Vox Sang 1994;66:117-21.
77. Draft guideline for quality assurance in blood establishments (Docket No. 91N-0450). Bethesda: Center for Biologics Evaluation and Research, Food and Drug Administration, US Dept of Health and Human Services, June 17, 1993.
78. Myhre BA. Crossing over of autologous and directed donor blood. Ann Clin Lab Sci 1992;22:343-52.
79. Kruskall MS, Glazer EE, Leonard SS, et al. Utilization and effectiveness of a hospital autologous preoperative blood donor program. Transfusion 1986;26:335-40.
80. Renner SW, Howanitz PJ, Bachner P. Preoperative autologous blood donation in 612 hospitals. A College of American Pathogists' Q-Probes study of quality issues in transfusion practice. Arch Pathol Lab Med 1992;116:613-9.
81. Yawn DH. Autologous blood donation programs. In: Rock G, Seghatchian MJ, eds. Quality assurance in transfusion medicine, vol 1. Boca Raton, FL: CRC Press, 1992:135-56.
82. Guidelines for autologous transfusion. I. Pre-operative autologous donation. British Committee for Standards in Haematology Blood Transfusion Task Force; Autologous Transfusion Working Party of the NBTS. Transfus Med 1993;3:307-16.
83. Yomtovian RA, Schrank JY, Betts YM, Kepner JL. Transfusion of previously donated autologous blood in a community hospital. In: Pineda AA, Taswell HF, eds. Autologous transfusion and hemotherapy. Boston: Blackwell, 1991:78-93.
84. Sazama K. Reports of 355 transfusion-associated deaths: 1976 through 1985. Transfusion 1990;30:583-90.
85. Dodd RY. The risk of transfusion-transmitted infection (editorial). N Engl J Med 1992;327:369-73.
86. Daniels N. HIV-infected professionals, patient rights, and the "switching dilemma." JAMA 1992;267:1368-71.
87. Gambino R. Most laboratory errors are system dependent—not people dependent (editorial). Lab Med 1989;20:123.
88. Taswell HF, Galbreath JL, Harmsen WS. Errors in transfusion medicine. Detection, analysis, frequency, and prevention. Arch Pathol Lab Med 1994;118:405-10.
89. Wenz B, Burns ER. Improvement in transfusion safety using a new blood unit and patient identification system as part of safe transfusion practice. Transfusion 1991;31:401-3.
90. Taswell HF. It's in the bag (or is it?) (editorial). Transfusion 1991;31:386-7.
91. Popovsky MA, Moore SB, Wick MR, et al. A blood bank consultation service: principles and practice. Mayo Clin Proc 1985;60:312-4.
92. Shulman IA, Lohr K, Derdiarian AK, Picukaric JM. Monitoring transfusionist practices: a strategy for improving transfusion safety. Transfusion 1994;34:11-5.
93. Kasprisin CA. Auditing into compliance (editorial). Transfusion 1994;34:5-6.
94. Glantz LH, Mariner WK, Annas GJ. Risky business: setting public health policy for HIV-infected health care professionals. Milbank Q 1992;70:43-79.
95. Recommendations for prevention of HIV transmission in health-care settings. MMWR Morb Mortal Wkly Rep 1987;36(Suppl 2S):2S-18S.
96. Update: universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus and other bloodborne pathogens in health-care settings. MMWR Morb Mortal Wkly Rep 1988;37:377-88.
97. Occupational exposure to bloodborne pathogens: final rule (29 CFR 1910.1030). Federal Register 1991:64175-64182.
98. Borowshy EA. Donor and employee safety. In: Kasprisin C, Laird-Fryer B, eds. Blood donor collection practices. Bethesda: American Association of Blood Banks, 1993:25-40.
99. Starkey JM, MacPherson JL, Bolgiano DC, Simon ER, Zuck TF, Sayers MH. Markers for transfusion-transmitted disease in different groups of blood donors. JAMA 1989;262:3452-4.
100. Petersen LR, Doll LS. Human immunodeficiency virus type 1-infected blood donors: epidemiologic, laboratory, and donation characteristics. Transfusion 1991;31:698-703.
101. Gerberding JL. Does knowledge of human immunodeficiency virus infection decrease the frequency of occupational exposure to blood? Am J Med 1991;91 308S-311S.
102. Nelsing S, Nielsen TL, Nielsen JO. Occupational blood exposure among health care workers: II. Exposure mechanisms and universal precautions. Scand J Infect Dis 1993;25:199-205.
103. Mast ST, Woolwine JD, Gerberding JL. Efficacy of gloves in reducing blood volumes transferred during simulated needlestick injury. J Infect Dis 1993;168:1589-92.
104. McGuff J, Popovsky MA. Needlestick injuries in blood collection staff: a retrospective analysis. Transfusion 1989;29:693-5.
105. 42 USC §12101 et seq.
106. Orentlicher D. Rationing and the Americans with Disabilities Act. JAMA 1994;271:308-14.
107. 28 CFR §36.208.
108. 29 USC §794 et seq.
109. *School Board of Nassau County Florida v. Arline* 480 US §273 (1987).

Roslyn A. Yomtovian, MD, Assistant Professor of Pathology, Case Western Reserve University School of Medicine; and Director, Blood Bank-Transfusion Medicine Service, University Hospitals of Cleveland, Cleveland, OH; address for reprints: Roslyn A. Yomtovian, MD, c/o Deanna Hines, AABB, 8101 Glenbrook Road, Bethesda, MD 20814.

Cynthia Kelly, Esq., General Counsel, Director, Government and Legal Affairs, American Association of Blood Banks, Bethesda, MD; current address: 6610B Jupiter Hills Circle, Alexandria, VA 22312.

Arthur W. Bracey, MD, Clinical Associate Professor, University of Texas Health Science Center, and Medical Director, Blood Bank and Transfusion Service, St. Luke's Episcopal Hospital, Houston, TX.

Sharon K. McCraney, Associate Director of Technical Services, American Red Cross Blood Services, South Carolina Region, Columbia, SC.

Stephen W. Renner, MD, Assistant Professor of Clinical Pathology, University of California, Los Angeles, and Chief of Blood Bank and Hematology Units, Wadsworth VA Medical Center, Los Angeles, CA.

Kenneth R. Williamson, MD, Consultant, Department of Transfusion Medicine, Mayo Foundation, Rochester, MN.

Safuh Attar, MD, Professor, Division of Thoracic and Cardiovascular Surgery, University of Maryland School of Medicine, Baltimore, MD.