

# Current Issues

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## PART 1: IMPACT OF AIDS ON BLOOD COLLECTION AND USE

Acquired immunodeficiency syndrome (AIDS) is a disease now shown almost conclusively to be of viral origin, with a high mortality rate (>40 percent of all diagnosed cases), and which is apparently transmitted through body fluids (e.g., semen, blood) through such means as sexual contact and intravenous drug abuse.

The disease is characterized by a profound disturbance of the immune system, with death usually due to extreme susceptibility to infections by organisms which rarely cause disease in persons with normal immunity (e.g., *pneumocystis carinii* pneumonia) and/or the development of a type of cancer (Kaposi's sarcoma) that is usually seen only in elderly or severely immunocompromised individuals.

The probable agent for AIDS attacks a type of white blood cell, T lymphocytes, which help to mediate the body's immune system through helping or suppressing the production of antibodies. It appears related to another virus which has been recently identified as the cause of human T-cell leukemia. The probable agent for AIDS apparently selectively infects and kills T-lymphocyte "helper" cells, whereas the T-cell leukemia virus infects T cells and, instead of killing them, turns them into cancerous leukemia cells (211,444, 476,488). (AIDS is examined in an OTA Technical Memorandum, "A Review of the Public Health Service's Response to AIDS" (in press).)

In the United States, the early AIDS cases were concentrated among homosexual and bisexual men, intravenous drug abusers, and persons of Haitian origin. As time passed, however, cases began to show up in hemophiliacs, and investigations of cases of unknown origin appeared to show a relationship between blood transfusions and subsequent development of AIDS (143). There was initial skepticism toward the conclusion that some AIDS cases were due to blood transfusions, but at a February 1984 meeting of blood banking representatives convened by the

Centers for Disease Control (CDC), there was agreement that the evidence was conclusive enough that AIDS could be and had been transmitted through blood products, that no further studies need be conducted to prove/disprove the association, and that studies to quantify and clarify the risks were needed.

Table 34 summarizes the percent of AIDS cases according to groups at risk as of January 1984. The "other" category includes some cases of apparent transfusion-related AIDS in infants, whose immune status is sufficiently different from adults so that CDC has classified these infant cases separately from adult cases. Some of these infants, however, either had transfusions or were children of known AIDS patients.

In an April 1984 telephone conference call with representatives of blood banking organizations, CDC reported that there were: 1) 43 adult cases of AIDS associated with blood transfusions, with an additional 10 cases in children; and 2) 33 cases of AIDS in hemophiliacs. CDC had completed its investigations of 13 adult and 7 pediatric transfusion cases. In 12 of the 13 adult cases, at least one donor was identified who was either in a high-risk AIDS group (e.g., homosexual or bisexual

**Table 34.—Centers for Disease Control's Characterization of Groups at Increased Risk for AIDS in the United States (percent of total reported AIDS cases as of Dec. 19, 1983)**

	Percent of total reported AIDS cases
Homosexual and bisexual men . . . . .	71
Intravenous drug abusers . . . . .	17
Haitians living in the United States . . . . .	5
Heterosexual contacts of persons at increased risk for acquiring AIDS . . . . .	1
Hemophiliacs . . . . .	1
Recipients of blood transfusions . . . . .	1
Other (unknown) . . . . .	4
Total . . . . .	100% (3,000 cases)

SOURCE: CDC, *Morbidity and Mortality Weekly Review*, Jan. 6, 1984

men) or who had an abnormal T-lymphocyte helper: suppressor ratio. At least one high-risk donor was identified in five of the seven pediatric cases with completed investigations.

The incidence of transfusion-related cases of AIDS is difficult to estimate because CDC traced blood donations as far back as 5 years in their search for a possible cause. CDC'S first report of an association of transfusions with AIDS, for example, stated that the first 18 cases they reported on were diagnosed during approximately a 12-month period (to August 1983), when over 3 million persons in the United States received transfusions. But most of these cases were transfused between 1979 and 1982, when the prevalence of AIDS was much lower than during late 1982 and early 1983 (143). An incidence rate based on the time of diagnosis would be 18 per 3 million persons transfused, or 6 cases for every million persons transfused. At a rate of approximately 10 million units of blood components transfused per year (518), there would have been approximately 2 cases of AIDS for every million units transfused.

Cases in hemophiliacs have occurred at a much higher rate. Estimates are that there are 15,000 moderate to severe hemophiliacs in the United States (6), and 5,000 more mild hemophiliacs (173), or a rate of about 1/500 for the 37 AIDS cases diagnosed as of June 1984.

Hemophiliacs have been at highest risk of all blood group recipients, probably through the use of Factor VIII (and Factor IX) concentrates. If AIDS is indeed a virus, and based on the histories of the transfusion-related AIDS cases (143), all blood components—whole blood, red cells, platelets, cryoprecipitate, and plasma—are also capable of transmitting the agent.

Several methods have been employed to screen out AIDS from the blood supply. These include: 1) donor screening in addition to those methods which were already employed, 2) laboratory tests to identify donors at risks for AIDS, 3) product recalls, and 4) attempts to inactivate the AIDS agent.

FDA, in consultation with the major blood banking and plasma derivative organizations, the National Hemophilia Foundation, the National

Gay Task Force, the Centers for Disease Control, and the National Institutes of Health, issued a recommendation in March 1983 to initiate the following procedures (566):

1. Educational programs to inform persons at increased risk of AIDS to refrain from blood or plasma donation. Persons at increased risk of AIDS were defined as follows: persons with symptoms and signs suggestive of AIDS, sexually active homosexual or bisexual men with multiple partners, Haitian entrants to the United States, present or past abusers of intravenous drugs (such intravenous drug abusers were already excluded by prior regulations), and sexual partners of persons at increased risk of AIDS.
2. Expanded medical screening of blood and plasma donors to identify individuals with early signs or symptoms of AIDS, with revision of standard operating procedures to include questions to elicit a history of night sweats, unexplained fevers, unexpected weight loss or signs of lymph node enlargement or Kaposi's sarcoma.
3. Examination of source plasma donors for lymph node enlargement by a physician (initially and annually), and by an adequately trained individual at each donation.
4. Measurement of body weight of source plasma donors prior to each donation to detect unexplained weight loss. If loss was detected, a physician's examination was recommended prior to continued plasma collection.

The sensitivities involved in screening high-risk donors are obvious; homosexual or other sexual activities and the use of injectable drugs are activities associated with a high degree of social stigma and illegal in many States. In negotiations surrounding the adoption of screening policies, spokespersons for the gay community have expressed fears about what the "stigma of bad blood" would do to a group already vulnerable socially, politically, and economically (66,322). To compound matters, it appears that the risk of contracting and transmitting AIDS is linked to the degree of sexual activity and number of sexual partners. Leaders of the gay community have ob-

jected to the use of the value-laden term, “promiscuity” (368). Gay physicians have cooperated and urged the adoption of a more restrictive definition of what constitutes a degree of sexual activity sufficient to contraindicate blood donation.

It has also been recognized that, while AIDS has been linked with male homosexual practices, women contracting the disease have been in other risk categories—e.g., sexual partners of bisexual men, intravenous drug users, or recent Haitian immigrants. Thus, gay women have continued to be safe prospective donors, and the blood banking community has continued to include them in appeals for blood donations.

As part of generalized public information campaigns about the risk of AIDS, the Public Health Service has included warnings about who should refrain from donating blood. Blood banking organizations such as the American Association of Blood Banks (AABB) have also waged their own public information efforts, aimed at both increasing awareness of high-risk donors and allaying groundless fears that AIDS could be contracted by simply donating blood (which involves a sterile needle that is disposed of after a single use).

In addition, many blood banks have introduced procedures which allow donors to privately indicate whether or not their blood donations should be used for transfusions, because such individuals may be especially reluctant to acknowledge their homosexuality or use of injectable drugs before their peers at school, business, or community blood drives. The New York Blood Center, for example, initiated a confidential form in February 1983 on which donors could indicate whether their blood could be used for transfusions or only for laboratory studies. A more common mechanism is to inform donors that they can call the blood bank after donating to indicate whether or not their blood should be used for transfusions. The Red Cross formally adopted such a mechanism on January 1, 1984.

For source plasma collectors, an additional recommendation from FDA was that plasma collected in geographic areas at high risk should not be used to manufacture the coagulation proteins. Manufacturers have ceased to accept plasma for Factor VIII and Factor IX products from prisons

and the cities of New York, San Francisco, and Los Angeles (Hollywood area) (162),

A number of commentators have expressed concerns that any system aimed at screening high-risk donors, rather than the blood itself, will be imperfect. In the early debates over whether potential benefits from screening questions outweighed the dangers of invasion of privacy, an AABB Transfusion Transmitted Diseases Task Force resolution stated, “In fact there is evidence that such questions, no matter how well-intentioned, are ineffective in eliminating those donors who may carry AIDS. ”

While it maybe too early to gauge the success of the screening procedures, some tentative initial assessments indicate that there has been a drop-off in donations by males between the ages of 18 and 35. Spokespersons for the New York Blood Center, for example, have reported a high degree of cooperation from the gay community, with whom they initially forged ties during the years of studies concerning transfusion associated hepatitis, when thousands of gay men were recruited as subjects (230). Blood bank recruiters have said that the same sense of civic responsibility that led to donating in the first place has convinced gay men to refrain from donating or allowing their blood to be used in transfusions (144).

On the user side, the National Hemophilia Foundation (NHF) (399) recommended that cryoprecipitate be used to treat newborn infants and children under age 4, newly identified patients never treated with Factor VIII, and patients with clinically mild hemophilia who require infrequent treatment. Similar recommendations have been made for Factor IX deficient patients when fresh-frozen plasma can be used instead of Factor IX Complex. No specific recommendations have been made between cryoprecipitate and Factor VIII for the treatment of severe hemophiliacs because of controversy over their advantages and disadvantages. Thus, the NHF recommends the continuation of early and appropriately intensive replacement of Factor VIII or Factor IX in the form of Factor VIII or Factor IX Complex at each hemorrhagic episode, for the approximately 90 percent of severe and moderately severe hemophiliacs now so treated in this country.

These recommendations came in the wake of a number of anecdotal reports that hemophiliacs were reducing the amount and frequency of administration of coagulation concentrates, foregoing treatment when indicated, or using smaller doses for bleeding crises. Such practices risk increasing the long-term morbidity associated with the disease, especially the orthopedic problems occasioned by bleeding into the joints, one of the most vexing problems of hemophilia. There have also been accounts of hemophiliacs declining necessary dental treatments or elective surgery, procedures which can require massive doses of coagulation products as a precautionary measure (s).

Plasma from a few donors subsequently diagnosed as having AIDS, or even from a single donor, has led to uncertainty over the safety of all the Factor VIII (and IX) concentrates derived from the thousands of plasma units containing the plasma from donor(s) with AIDS. All four commercial manufacturers of coagulation proteins, as well as the Red Cross and the New York Blood Center, have voluntarily withdrawn lots of Factor VIII or Factor IX upon learning that an AIDS victim had donated plasma used in their preparation.

The potential dimensions of this problem are enormous. Because of the preclinical, asymptomatic phase of AIDS, donors could give many times before becoming aware of having contracted the disease. In one recall case, an Austin, TX, man had sold plasma to a commercial center 50 times before being diagnosed as having AIDS. The process of pooling thousands of products also contributes to the need to quarantine a great deal of the product; the largest of the voluntary withdrawals involved enough Factor VIII to represent 500 patient-years of treatment (434).

All four manufacturers of coagulation factors have also recently received FDA approval to market heat-treated Factor VIII. These preparations have been shown to reduce the infectivity of hepatitis viruses and a variety of marker viruses added prior to the treatment process, with the hope that viruses from other heat-sensitive classes such as the retroviruses (in which the proposed AIDS organism belongs) may be similarly affected. The heat treatment is also estimated to de-

crease potency of these preparations by about 10 to 20 percent (162).

While donor screening has been most controversial among the affected donor groups, the methods that have raised the most controversy among blood bankers have been attempts to screen out AIDS from the blood supply through the use of laboratory tests. No specific test for AIDS is available, although one may become available in the relatively near future if the tentative identification of an AIDS virus is confirmed and tests can be devised to be used on a mass scale as promised (256). In the absence of a specific test for AIDS, attempts have focused on "surrogate" tests. These are of two types: 1) detection of abnormalities associated with AIDS or the preclinical stages of the disease, and 2) evidence of past infections with diseases that have a high incidence in the same population groups that are at increased risk for AIDS. Both of these types of surrogate tests will be positive in a much higher number of people than actually have the AIDS agent.

The total costs associated with surrogate tests include the cost of testing each individual unit, the loss of blood which tests positively, and higher recruitment costs associated with seeking donors to replace those excluded. Moreover, tests purporting to reveal abnormalities implicated in the preclinical stages of the disease raise questions about what kind of information to share with those who test positively. Conditions other than AIDS can lead to abnormal test results in tests of the first type. For example, the Stanford University Blood Bank now tests all whole blood donations for the T-lymphocyte helper: suppressor ratio. About 1 to 2 percent of collections are positive and discarded, but donors are not deferred permanently, since short-term virus infections can also cause an abnormal ratio (445).

In the second type of surrogate test that tests for past infections with other diseases, the diseases tested for have much higher incidence than known for AIDS. For example, in May 1984 Irwin Memorial Blood Bank in San Francisco initiated the test for antibodies against hepatitis B core antigen (anti-HBc)(indicating past infections with hepatitis B) and expects that deferrals will increase

by 5 to 7 percent because of positive tests (445). (Irwin expects that the test will also help to prevent non-A, non-B hepatitis transmission, another infectious agent that so far has not been identified specifically, although current research indicates it is a virus.) Cutter, one of the four fractionators of plasma, also announced at approximately the same time that it also would use the anti-HBc test and expects that approximately 15 percent of its donors will have positive tests. Cutter plans to use their plasma only in producing albumin and immune globulins, which have not been implicated in AIDS (137).

A study group of the Food and Drug Administration's (FDA) Blood Products Advisory Committee has also been studying whether surrogate tests, specifically, the anti-HBc test, should be instituted for all whole blood and plasma collections, with the majority believing that the test was not appropriate as a means of identifying AIDS high-risk group members. This group also recommended in March 1984 that another surrogate test be studied in pilot tests. This test would be for beta-2 microglobulin, a cell surface protein component of the immune system that has been found to be elevated in patients with AIDS. Finally, the study group also recommended that a pilot study be conducted to measure the effectiveness of procedures by which plasma donors could privately indicate that their plasma should not be used in the manufacture of coagulation products.

Pressure to adopt some type of surrogate test may have been temporarily alleviated by the announcement on April 23, 1984, by the Department of Health and Human Services of its claim to identifying the AIDS virus, and its promise that a blood test would become "widely available within about 6 months," which should "identify AIDS victims with essentially 100 percent certainty" (256). Whether or not this expectation will be realized should be known soon.

Pressure to institute some type of laboratory screening test reflects the preoccupation with safety with blood resources, with costs a secondary consideration. This is manifest in the decision by some blood banks and plasma fractionators to use surrogate tests, despite their high "false positive" rates for AIDS, loss of donors, and the

increased recruitment effort needed to replace excluded donors. Blood bankers have also noted that costs and benefits must be weighed in the balance and that, moreover, the potential costs of not performing surrogate tests include those associated with the treatment of additional AIDS cases and the potential for lawsuits arising from transfusion associated AIDS.

Assurances of safety from surrogate tests, whatever their validity, can also become factors in competition for patients. For example, an additional reason for San Francisco's Irwin Memorial Blood Bank's adopting the anti-HBc surrogate test was Stanford University Blood Bank's use of another surrogate test, the T-lymphocyte helper: suppressor ratio test. Apparently, the use of a surrogate test by Stanford and not by Irwin was perceived by some patients and doctors as reflecting a "safer" blood source at Stanford (445).

For the longer term, costs may become a more prominent factor in decisions to adopt additional safety measures because of prospective payment systems that are currently being implemented (discussed in a subsequent section of this chapter). Even if a "guaranteed" screening test for AIDS becomes available, the question still remains whether it should be required of every whole blood and plasma collector, or limited to high-risk whole blood collection areas and to plasma supplies, the latter because of the pooling of thousands of units prior to fractionation into coagulation products.

The impact of AIDS has had other effects on the blood supply besides the search for good methods to screen out AIDS. Interest in autologous donations, where a patient banks his/her own blood prior to elective surgery, has increased dramatically. Autologous donations have long been supported by the blood banking community as the safest method of transfusion, and indeed, a substantial portion of requests for autologous transfusions probably originate with physicians rather than patients, since in many institutions physicians must give their written permission for such a request and in many cases must point out to the patient that it is an option (445). Nevertheless, their potential application is limited when contrasted against the total number of transfusions.

Predepositing one's own blood requires knowledge in advance of the nature and extent of the elective surgery anticipated and, furthermore, the patient must be healthy enough to withstand the blood donation process (often entailing the donation of three units of blood in the month prior to surgery). The blood bank, for its part, must be prepared to meet the logistical requirements necessary to make the patient's own blood available at the time of the operation. And even when these steps are successfully undertaken, the process can be undermined should the patient require more blood products than he or she was able to predeposit.

Use of the patient's own blood has also been achieved through means other than deposits in advance. These efforts have primarily been undertaken for those, such as Jehovah's Witnesses, whose religious beliefs preclude them from accepting transfusions of blood products (121). Intra-operative salvage and postoperative collection of shed blood have been used in surgery following traumatic injury and in vascular, cardiac, and orthopedic surgery. Devices have been developed for collecting salvaged blood for reinfusion as whole blood or as "washed" red cells. The AIDS crisis has given new impetus to development of such techniques.

Fear of AIDS has also led to an increasing number of requests for "directed donations"; i.e., the transfusion of blood from specific individuals, usually family members or friends, rather than using a product from a general inventory. Directed donations were the standard mode of operation until technological advances in this century made storage and preservation of blood products possible through maintenance of a constant inventory, and typing and crossmatching of blood enabled safe exchange of blood between strangers with the same blood type. The director of one of the Nation's first blood banks described the importance of these advances in a 1938 article. "The advantage of the 'blood bank' over the previous method is obvious. [It] dispenses with the commotion occasioned by calling to the hospital a horde of excited relatives before a suitable donor can be found" (176).

Today, directed donations are viewed negatively by most blood bankers because of the potential for disruption of the blood collection and distribution system and because of lack of evidence that such donations are indeed safer. Opponents of directed donations have argued against setting up a two-tiered system of blood, one allegedly safer than the other. Furthermore, there has been concern about the effect on the donor pool; will prospective or regular donors refrain from giving in order to be eligible to give should an emergency arise for a friend or family member? Reflecting these concerns, the American Red Cross, AABB, and the Council of Community Blood Centers have issued a joint statement counseling against the establishment of directed donation programs (14) which was echoed by the College of American Pathologists (129) and the American Medical Association (38).

Individual hospitals and blood banks have had to grapple with the question of whether or not to allow requests for directed donations, either as a matter of institutional policy or on an ad hoc basis. Many hospitals have tried to discourage the practice either through scientific or moral suasion or bureaucratic intransigence. However, a few individual blood banks have instituted directed donation programs under pressure from patients, donors, and clinicians (445). In Philadelphia, Thomas Jefferson University's blood bank established a directed donation program at the urging of cardiac surgeons (whose patients commonly receive multiple units of whole blood or red cells).

Irwin Memorial Blood Bank, located in San Francisco, where AIDS has been a particular concern, adopted a program in June 1984 to allow directed donations as a matter of formal institutional policy to be made known to all prospective transfusion recipients. Irwin's somewhat grudging acceptance of the directed donation concept is reflected in its advice to patients and in procedural barriers it erects before allowing such donations to proceed. Patients are advised "that blood from directed (family and friend) donors is *at best no safer* than blood from other volunteer donors (and) there is actually a danger that directed donations may be less safe. "



If patients insist on a directed donation, their physician must place the request at least a week prior to the anticipated transfusion and the patient's friend or relative must undergo an initial screening and testing procedure at the cost of an additional \$15. If the potential donor passes the screening test, he or she must then return on a separate occasion to actually make the donation. The donor is told of the importance of forthright answers to screening questions and told that if use of the blood turns out not to be warranted for the particular individual, it will be turned over to the general inventory. Designated donors are encouraged to return and donate with no strings attached.

Special concerns about safety have also arisen in the pediatric context, especially with treatment of neonates in the intensive care setting. Blood replacement is a frequent occurrence in this population. In addition to such reasons for transfusions as hemorrhaging, arterial blood gas evaluations and other laboratory tests require the frequent withdrawal of blood for monitoring. Although this may be in small amounts of 5 or 10 ml at a time, in the aggregate it can amount to a significant proportion of the blood volume of tiny neonates. Particularly poignant cases of the deaths of very young children from transfusion-associated AIDS have received a great deal of media attention (325). As mentioned, the response to pediatric AIDS cases is complicated by problems in defining what actually constitutes AIDS in young children because of their naturally immature immune systems.

Some of the parents involved have emerged as articulate proponents of more vigorous donor screening methods, surrogate tests and limiting the number of donors for multiple transfusions when pediatric patients are involved. They have also criticized what they perceive as the dilatory response of the blood banking community (especially the voluntary sector) in adopting screening procedures, and an inadequate and delayed response in funding studies related to transfusion-associated AIDS, especially in pediatrics.

The impetus for directed donations from physicians or patients has also resulted from concerns that whatever the actual risks of contracting AIDS

from a blood transfusion may be, the perceived risks may be no less important. A review of the directed donation program at Cedars-Sinai hospital in Los Angeles concluded that "[w]e function with a philosophy that incorporates a concern for the patient's psychological responses to illness, as well as his need for blood. . . . [B]y providing these very frightened patients with the knowledge that the blood to be received is from their chosen donors . . . [we] enhance their general well-being and eventual recovery" (452).

Directed donors have also been described as an additional source of donors; they may not have been active donors in the past. Family and friends can sometimes meet the majority of the patient's need for blood, thereby reducing the demands on the general inventory. And because the patient effectively supplies the donors, there is little or no cost associated with recruitment.

While directed donation programs may not be disruptive if limited to individual blood banks and for individual patients, a more serious case is one in which a donor gives blood but specifies that it may be used only for another member of one's organization. In this case, entire sets of blood might be tied up, which is somewhat reminiscent of the nonreplacement fee or blood credit system—but with the additional feature of restricting physical access to the blood and raising the specter of greatly increased outdating and wastage. According to the administrative director of the Greater New York Blood Center, "If people start to set up separate pools . . . , we'd see little packets of donors and eventually the blood banks would be destroyed" (341).

One example of blood banking's response to such suggestions was triggered when the president of a country club civic association in Long Island, NY, sent a letter soliciting members to join a special blood donor registry so that the risk of contracting AIDS might be reduced by "obtaining blood directly from people you know." When accounts of this effort appeared in the newspapers, local blood banking officials contacted the organizers, concerned about their basic idea of "establishing a registry of 'pedigreed donors' without knowing anything about the donors' actual medical background and history." When representa-

tives of the civic association were given a tour of the local blood bank and apprised of the donor screening policies, they withdrew their suggestion and instead sponsored a conventional blood drive with no strings attached (432).

Directed donations built up around organizations instead of individual patients have great potential for disrupting the present, well-balanced system of blood supplies. In a recent AABB survey on public perceptions of AIDS and the blood supply, the largest percent of those who donated regularly did so to contribute to a company blood drive (33.6 percent). Currently, companies allow employees to donate blood during working hours, and many firms give additional time off as a reward. Thus, the potential is present on the part of the company or even its employees to demand a directed donation program.

Legislators in several States (Florida, Georgia, Kentucky, Washington) have also introduced bills requiring blood banks to accept directed donations, but, in the face of concerted opposition by blood bankers, none of these legislative initiatives has progressed very far. (One related and similarly unsuccessful proposal from a New Jersey State senator would have made it a criminal offense to misrepresent one's health status or membership in a high-risk group.) The development and availability of a specific screening test for AIDS, however, should do much to alleviate the safety concerns that underlie much of the current interest in directed donation programs.

But while awaiting confirmation of the identification of the viral agent associated with the transmission of AIDS and the development of a definitive screening test, there remain a number of practical and ethical questions for blood bankers—and particularly for researchers tracking down the blood connection. Perhaps the most intractable questions involve how to deal with medical information which is riddled with uncertainty or information which fails to point up any possible therapeutic responses. Gerald Sandier of the Red Cross put it this way: "I have had 10 years of explaining tests to people. I want to know how you will deal with those 5 percent of the normal population who will be positive for anti-HBc. . . . How can you convince people that their blood is no good, but they're healthy?"

Questions of confidentiality and the need to balance privacy interests against public health concerns, while not unique to AIDS, are raised in sharper relief than in any other area of medical practice and research. Recent scientific breakthroughs may give these questions a new twist. In May 1984 the Red Cross announced plans to conduct pilot tests of donated blood for antibodies to the HTLV-III virus—the presumed agent of AIDS. Development of such a test carries with it immediate concerns about scale-up and availability, specificity and sensitivity, as well as ethical questions about the use of information revealed by the test. It remains to be seen whether the test will be simple and cheap enough to be readily available on a scale massive enough to obviate questions about who should have priority among potential users. In addition to blood banks generally, blood banks in high-risk areas and commercial plasmapheresis centers, additional millions of potential test users include members of groups at risk of contracting AIDS—male homosexuals, intravenous drug users, and Haitians.

Also unclear are the implications of a positive test. Red Cross officials have predicted that positive findings of an AIDS screening test will be dealt with much as hepatitis B findings have been in the past. Donors who tested positively would be informed by a letter, which would include an offer to make the information available to the donor's physician. The donor's name would then be added to a registry of permanently deferred donors, with the reasons for the deferral encoded in a format strictly limiting their availability. Additional questions arise because in a number of States, AIDS, like some other communicable diseases, must be reported by physicians to public health officials. Should these same reporting requirements apply in similar fashion to positive results of an AIDS test even if it is not a definitive diagnosis of the disease? These are among the issues confronting those who seek to develop, market, and implement an AIDS screening test. When announcing its plans for pilot testing, the Red Cross also stated that it was convening an ethics advisory panel to help sort through this thicket of questions.

Related dilemmas concern how to divulge information uncovered in the course of epidemio-

logical investigations by public health officials. What should high-risk donors be told once they have been implicated in an AIDS case? Should other recipients of blood products from these same high-risk donors be told that they, too, are at risk of contracting AIDS (or as a way to prevent unwarranted fear, should the information be divulged only to their treating physicians)? Local public health officials have shared the names of AIDS victims in high-risk areas with local blood banks, so that it might be confirmed whether or not they donated and, if so, who received their blood products (e.g., the San Francisco Health Department and the Irwin Memorial Blood Bank). (Federal regulations require that records of blood donors who donate products for human use be kept for 5 years. )

Is this practice being conducted with the necessary degree of regard for the protection of patient confidentiality? Should it be expanded in scope? Do the proper authorities have access to names and other patient identifiers? Should social security numbers ever be used in this process? Are public health officials doing enough to assure that AIDS victims have not failed to mention if they were blood or plasma donors, either because they did not recall when and where they donated or because they fear further stigma?

These are representative of the kinds of ethical issues confronting blood bankers, public health officials, and especially researchers. (A task force of the bioethics research group, The Hastings Center, has recently completed a set of guidelines for confidentiality in AIDS research. These guidelines specifically eschew consideration of concerns specific to blood banking. These questions are being addressed by CDC and the National Heart, Lung, and Blood Institute in the course of designing protocols to test research hypotheses. )

Finally, while many areas experienced a decrease in blood donations in 1983, there does not seem to have been major or systematic shortages of blood supplies. The Red Cross, for example, had been experiencing yearly increases in collection of about 5 percent prior to 1983, but in 1983, no increase was noted. However, demand was about equal to supply, and Red Cross analysts noted that supply was dependent on demand, and that most of the decreased demand could be attributed to reduced hospitalization and surgery (302).

This decrease in demand was also noted elsewhere. The Gulf Coast Regional Blood Center reported a 5-percent decrease in red cell use and a 3.5-percent decrease in overall blood component use in 1983 compared to 1982. The single largest contributing factor was a severe economic recession in the gulf coast area, with decreased insurance coverage and elective surgery. But many patients were questioning physicians about transfusions, and AIDS played a large role in reduced use (527). Similar conclusions were made for the hospitals supplied by San Francisco's Irwin Memorial Blood Bank. Hospitals supplied by Irwin transfused 3 percent fewer whole blood and red cells in 1983 than in 1982, and there was no serious problem with supplies even though donations dropped 4.6 percent in the same period.

Some of the decline in demand probably reflected a tendency for patients to postpone elective surgery while the economy was poor. However, the steady decline in red cell use throughout all four quarters of 1983, when the economy was improving, suggests that fear of contracting AIDS may also have been a contributing factor in the decision to postpone surgery and in encouraging physicians to be slightly more conservative when ordering blood for transfusions (445).

## PART 2: COORDINATION OF BLOOD RESOURCES

Coordination of blood resources is complicated by the pluralistic system of blood services that has developed in this country since World War II. To date, efforts at coordination have focused on two

aspects of blood delivery. One is the coordination of all blood services within a given geographic area; this effort has been termed **regionalization**. The second area of coordination involves provid-

ing excess blood to other blood providers who are occasionally or chronically deficient; this phenomenon of cooperation is called resource sharing.

Regionalization is not acknowledged by all to be the best approach to managing blood supplies. One of the recurring questions is the benefit gained from participation in the American Blood Commission's regionalization recognition program. Another recurring debate centers on the issue of centralized blood services v. hospital-based services, or some combination of the two. In addition, there are external forces, such as health care cost containment efforts, which are just beginning to have an effect on regionalization efforts.

The need for resource sharing is probably the single aspect of blood delivery which is not seriously debated within the blood services community. Rather, the need for a single resource sharing system has been the issue, given the existence of two parallel, though largely successful, systems—run by the American Association of Blood Banks and the American Red Cross.

## Regionalization

Essentially, regionalization is a term used to describe the local coordination of all facilities and organizations involved in blood collection, distribution, or use in a given geographic region. Generally, regionalization includes provisions for cooperation with other regions, thus linking regional blood programs into a national resource sharing program.

Many regions have been able to meet their own blood needs completely, relying exclusively on volunteer donors and satisfying the demand for blood from local practitioners. While some areas of the country are still concerned about meeting local blood needs, other regions are concentrating on the **centralization** of blood services within regions (i.e., the consolidation of small-scale blood banking operations into a central blood center).

On the whole, within any region of the country, a patient who needs blood will receive it, but there still remain the questions of efficiency and cost. There are many groups operating within each region. Should the plurality of the present system be left as is, because it produces accept-

able products at a sufficient level, or is there a better organizational framework for the provision of blood products at lower cost?

Since the formation of the American Blood Commission in 1975, the ABC has supported regionalization as the most logical way to improve blood services in the United States. The ABC recognized that there were effective, high-quality, regional blood programs in a few areas of the country, but felt that a national program was needed to improve the fragmented and uncoordinated blood services in other areas. From the start, the ABC regionalization program was conceived and implemented so as to preserve the roles of the many participants in blood banking. It has improved relations in regions in which a strong central blood service needed more formal and effective communications with its clients, and in doing so, maintained the autonomy of all participants with respect to management of the regional blood resources (507). But in less centralized regions, changing the roles of the participants or closing small operations have often been opposed.

Since the ABC has no enforcement mechanism, participation in the regionalization program has always been voluntary. In order to support the regionalization program, the ABC charges application and recertification fees to regions desiring to receive recognition.

The regionalization program sets forth criteria for regional associations which distinguishes regional associations from regional blood programs and provides a mechanism for areas wishing to be recognized to form such cooperative arrangements. The recognition criteria contain specifications in the following areas:

- governance,
- management,
- donor recruitment,
- inventory control,
- service area,
- interregional relationships, and
- range and quality of services.

For instance, the criteria require that the governance of a regional association shall provide for active participation of five interest groups:

1. donors;
2. blood centers, or the facility (ies), in the re-

- gion which perform the functions of collections, processing, storage, and distribution of blood;
- 3. hospital transfusion services;
- 4. physicians who provide direct patient care; and
- 5. the patients who receive blood.

Participation by these five groups is in contrast to a regional blood program, which usually involves only blood collection and distribution programs and perhaps hospital transfusion services. Participation of all these groups is often considered to be the essential difference between a recognized region and other regional blood programs.

Among other goals, the criteria state that the regional association should take an active role in inventory control and the redistribution of blood according to need within the region, and provide for cooperation with other regions in cases of unexpected need. Also, rather than require a particular approach, the criteria specify that donor recruitment should be philosophically coordinated within a region (i. e., either individual or community responsibility, ) so as to prevent donor confusion. The regions are also required to provide a specific range of services within acceptable quality limits (e.g., the provision of a physician available for consultation on difficult blood problems on a 24-hour basis) and to do as much as possible to promote good transfusion medicine (34).

In order for a region to receive official ABC recognition, it must pass through a four-phase application procedure evaluating a variety of operational and organizational criteria. In addition to an application fee of \$1,500, regions must supply application materials—including bylaws, financial statements, operating reports, etc.—and host a site visit by members of the ABC regionalization committee. Once recognized, a region must be recertified every 5 years (30).

As of October 1983, the ABC had fully recognized 43 regions, with 29 additional regions somewhere in the application process. These regions are located all across the country, and the ABC estimates that 50 percent of the Nation's blood supply is collected through regions participating in the regionalization program (31b). Despite these

accomplishments, however, there are questions as to the need for and the effectiveness of the ABC regionalization program.

Many criticisms of the ABC regionalization program stem from ABC's lack of power. ABC was conceived as a "private sector" organization "charged with carrying out public policy but lacking enforcement powers." The ABC never received a Federal charter. As a result, ABC programs are voluntary, and ABC recognition carries with it no legal status. The fact that "recognition" rather than certification is used to achieve compliance testifies to the difficulties of the ABC as an unofficial body in exerting its influence (601). Nevertheless, the ABC contends that the program provides an incentive to regions who voluntarily choose to regionalize and provides the technical assistance and advice to complete the project successfully.

The New York Blood Center (NYBC), one of the largest blood centers in the country, has opted not to pursue ABC recognition. In 1958, the New York Academy of Medicine Committee on Public Health realized that there were serious deficiencies in the safety of the blood supply and transfusion practices. Foremost among their recommendations were the steps which resulted in the NYBC. Years later, when the ABC was beginning its regionalization program, the NYBC was thriving and chose not to participate.

Few would argue that the NYBC is in any way inferior as a result. However, in 1978, the same committee of the New York Academy of Medicine examined the progress made toward the goals enunciated 20 years earlier. The main problem which remained to be solved was attainment of a good cooperative working relationship between the Blood Center and the hospital transfusion services; hospital blood bank directors felt that they did not have any voice in the operation of the blood center. Despite the appointment of advisory committees to the Blood Center, the NYBC management tended to accept only advice with which it agreed. Thus, hospital blood bank directors felt obliged to form their independent incorporated Council of Blood Bank Directors.

In an attempt to resolve this problem, the same New York Academy of Medicine committee con-

vened a subcommittee to explore the possibilities for developing a regional association more or less in accordance with ABC regionalization recommendations. Over the course of the next year, a compromise proposal, introduced by the representative of Blue Cross/Blue Shield of Greater New York, was finally approved by all participants, excepting the representative of the NYBC. The Blood Center objected to the portion of the proposal which called for a Council with its governance independent of the NYBC. To date, the impasse remains.

In the meantime, the New York Academy of Medicine Committee on Public Health has appointed a subcommittee to observe and report annually; this committee's charge is sufficiently broad to monitor all aspects of blood supply and transfusion services. This situation provides an example of a region which functions effectively in most respects but lacks a mechanism to resolve problems between the blood bank and its users (360).

Further, due to the cumbersome and expensive four-phase application procedure, some regions with strong regional blood programs had little incentive to gain ABC recognition, given the costs and effort required to acquire it. Some strong regional systems, such as the Puget Sound Blood Program, have not seen a need for such formal recognition, while other areas have not applied but have benefited from the information made available through the program and the knowledge gained from activities, successes, and failures of other regions. Because of this latter fact, perhaps the ABC regionalization program deserves more credit than the statistics indicate; and perhaps the program has provided assistance to those who needed it most (517).

Others have criticized the inconsistency with which the ABC confers recognition. For instance, in some places, autonomous functioning of small local blood banks which refused to be integrated into larger regional programs continued, but the regions were "recognized" nevertheless (601). In other areas, regions were allowed to apply for recognition without the participation of many of the users of blood.

In one notable instance, a region was allowed to apply for ABC recognition without the inclusion of the region's major blood supplier, the Red Cross, in the formal regionalization plan. The Washington, DC, Metropolitan Region has largely resolved its blood supply problems. Now, the Red Cross supplies the majority of blood in the area, supplemented by the Metropolitan Washington Blood Bank (MWBB), and some hospitals continue to be largely self-sufficient in the collection and processing of whole blood, red blood cells and platelets, as well as basic laboratory services. Only 2 percent of the area's blood supply is imported from outside the region. Several groups in the Washington area have applied for ABC recognition in an attempt to solve the problem of local coordination, but have reached an impasse as the major area supplier, the Red Cross, sees itself as a successful regional blood program (509).

In other instances, attempts at obtaining ABC recognition have stalled because of continuing territorial battles between blood programs. For instance, both the South Florida Blood Service and the Broward County Blood Center have expressed interest in the ABC regionalization program, but the two blood centers are still in the midst of a dispute over blood collection within Broward County. The competition for donors between the two blood centers has attracted the concern of the community, and efforts are under way to encourage a compromise. As a result, attempts at recognition have been tabled until the dispute is resolved (465; 532).

A report completed in 1981 under contract to NHLBI, evaluating the first 2 years of ABC's regionalization program, arrived at a much more positive conclusion. The analysis concluded that the regionalization program did provide incentives to improve, and the associations recognized by the ABC did meet the regionalization criteria, which were consistently and fairly applied. It concluded that the regional associations demonstrated evidence of both interregional resource sharing and regional self-sufficiency, and that "most regional associations include a high proportion of the total number of blood service establishments

in the region. " Generally, the regions do not conform to political divisions, but rather are built around existing blood center operations. The report also noted that plasmapheresis centers do not participate, although they may conduct substantial operations within a region (32).

Finally, there have been some concerns about possible antitrust allegations of "price-fixing" or "restraint of trade" on the local level as a result of regionalization (364), although there has been no litigation on this issue to date. The problem of antitrust action on a national level as a possible consequence of the Resource Sharing Agreement is currently being addressed by the ABC and its legal counsel. (See subsequent discussion. )

In conclusion, now that supply has been largely stabilized and inventory is not the central concern, efficiency and participation in decisionmaking by more than representatives of blood banks have become primary goals in regionalization efforts. The role of ABC's regionalization program has been to provide the catalyst and information for such regional efforts. It appears that each region will solve its problems on an individual basis, gaining from the experience of other regions and not necessarily pursuing ABC "recognition" as an end in itself.

## Resource Sharing

Over the past 30 years, there have been several attempts at interorganizational resource sharing. The first system has operated under the auspices of the AABB since its beginning in 1951 and is called the Clearinghouse Lifeline Program. In essence, the Clearinghouse serves as a facilitator in the exchange of blood or blood credits between blood banks, blood centers, and hospital blood banks or transfusion services. For the most part, the Clearinghouse serves regional blood centers, although it serves any AABB accredited facility which agrees to the conditions of participation, including facilities which are not members of the AABB.

In 1955, the Joint Blood Council, a short-lived group formed by the AABB, American Red Cross, American Medical Association, American Hospital Association, and the Society of Clinical

Pathologists, attempted to develop a cooperative interorganizational reciprocity blood program between the AABB and the ARC. The committee's proposal was never enacted, as the Red Cross representative indicated that the ARC Board of Governors would not approve the plan (18). The Red Cross then instituted its own national reciprocity plan for Red Cross blood centers, the Central Exchange Program, based in Washington, DC,

In 1958, negotiations reopened between the AABB and the ARC in another attempt to reach a sharing agreement. Finally, in 1960, an agreement for an interorganizational reciprocity program was reached between the AABB and the ARC. The agreement became effective May 27, 1961, and the two organizations operated under a series of sharing agreements which differed only in terms of fees, until 1976, when the Red Cross withdrew over concerns about nonreplacement fees. Upon the withdrawal, ARC formalized its sharing program, which acquired the name "Compass. "

Most recently, the major collectors of blood in the voluntary sector, and the American Blood Commission, attempted to arrive at a comprehensive resource sharing agreement. The Resource Sharing Agreement (RSA) was a proposal for a coordinated blood distribution arrangement between the American Blood Commission (ABC), the American Association of Blood Banks (AABB), the Council of Community Blood Centers (CCBC), and the Red Cross.

In late 1979, the Red Cross requested a Business Review from the Department of Justice for the proposed Resource Sharing Agreement (328). The antitrust considerations relevant to the RSA were price-fixing and illegal boycotting. The agreement contained provisions for shipping, processing, and other charges involved in the movement and sale/exchange of blood and blood products. Further, the system included an indemnification account and replacement deposit fee (responsibility fee, or nonreplacement fee). As a result, the Red Cross was concerned that a civil suit might be brought against it.

Representatives of the Justice Department's antitrust division expressed the view that the RSA

would not be challenged because it contained no enforcement mechanism for violation of the agreement. Litigation would be difficult, and a plaintiff would be forced to prove a boycott (330).

The boycotting concern was raised by ABRA in a letter from its general counsel to the general counsel of the American Blood Commission. The letter of May 3, 1983, charged that the RSA would implement a group boycott against producers of nonvolunteer blood products (meaning source plasma collected and/or fractionated by ABRA members). ABRA's argument was that as long as the FDA licensed these products, any contract limiting their purchase would be in violation of the antitrust statutes. The February 19, 1982, draft of the RSA stated that "only blood obtained from voluntary donors and labeled in accordance with applicable law will be shipped." The December 15, 1982, draft replaced the volunteer clause with . . . (blood) procured and processed in conformity with the National Blood Policy . . . " However, ABRA maintained that the National Blood Policy was and is synonymous with volunteer blood and that the result would be the same.

Because of the threat of civil litigation, the Red Cross refrained from joining in the RSA during the May 3, 1983, meeting at which the agreement was to have been signed. The December 1982 draft of the agreement was signed by the ABC, the AABB, and the CCBC but has not been implemented, although individual members of the AABB and the CCBC utilize the Clearinghouse. In addition, the Resource Sharing Council, under the auspices of the ABC, continues to meet in an effort to continue the dialog between the organizations on resource sharing. Despite the Red Cross' decision not to participate, the Resource Sharing Council invited them to attend as observers, if they so desired, but the invitation was declined. Most recently, representatives of the ABC and the CCBC attended a regular meeting of the AABB Clearinghouse committee as observers.

Even without implementation of the Resource Sharing Agreement, and without a single coherent national sharing system, regions with blood shortages are able to meet their needs. Individual blood centers contract with other blood centers outside

of the formal mechanisms of the Clearinghouse or the Red Cross, as well as within them. For instance, the South Florida Blood Service (SFBS) has been undergoing a huge transition over the past 5 years in its switch from paid to volunteer donors. As part of the transition, the region began importing exclusively volunteer blood from other regions in order to supplement the growing local collections from volunteer donors.

Over the years, the SFBS has decreased its percentage of imported blood, completely eliminated the use of paid blood, and increased its local collections from volunteer donors. The management of the SFBS managed to meet the region's blood needs through a combination of contracts with both Red Cross centers and independent regional blood centers, use of the AABB Clearinghouse, and supplementation via ad hoc shipments.

In some regions, there are even local clearinghouses which serve functions similar to the AABB's. For instance, the Metropolitan Washington Blood Bank (MWBB) was formed by hospitals over 20 years ago to receive daily inventory reports and to coordinate blood movement between the hospitals. Today, the MWBB continues to serve that function; in addition, it imports needed blood from outside the region and participates in the AABB Clearinghouse. In August 1983, the MWBB, after deciding that the region's blood needs were still not being met locally, as evidenced by the net import of blood into the region, began its own blood collection program. The Metropolitan Washington region continues to be dominated by the American Red Cross, which controls approximately 90 percent of the local blood supply.

### **American Association of Blood Banks**

In 1979, the AABB National Committee on the Clearinghouse developed its current program, whereby blood banks may participate on a blood credit-debit and/or fee-only basis. The Clearinghouse Lifeline Program consists of two alternative plans for members: the Blood Replacement Exchange and the Blood Cooperative Programs.

Participants in the Blood Replacement Exchange Program ship and receive blood under a debit/



credit accounting system, and accept and issue blood credits, if applicable. Routine inventory surpluses and shortages are reported daily to the District Clearinghouses, which match up compatible blood banks for inventory adjustment shipments. Also, members who charge nonreplacement fees may transfer credits through the Clearinghouse. In addition, the resources of the Clearinghouse are available to alleviate emergency shortages. Transactions are settled via monthly statements, which yield a net debit or credit balance owed by the participant. In 1982, 96 percent of the Clearinghouse transactions were through the Exchange Program, as opposed to the Cooperative Program. In the Blood Cooperative Program, blood banks operate on a fee-only basis.

The Clearinghouse also coordinates payment for any exchanged blood or credits. The Clearinghouse charges a \$0.40 fee for each transaction to both the shipper and the recipient of the blood (or credits) in order to cover the costs of operating the service (16). Payments for blood are made directly between the shipping and receiving blood banks, although the Clearinghouse maintains records of all transactions and provides monthly statements which summarize the amount of blood credits or money owed by individual participants.

The Clearinghouse sets a standard fee for blood obtained through it, unless both parties to a transaction agree to another fee (usually the slightly higher regular unit charge of the shipping blood center). Transportation costs, as of fiscal year 1984, must be split between the parties of a transaction. This change was instituted by the AABB Board of Directors on the premise that both facilities benefit from the shipment. The shipping bank is able to outlet surplus blood that may otherwise outdate on their shelves, and the receiving bank is able to obtain type-specific blood needed to meet a blood shortage (259). The Clearinghouse will also arrange for long-term inventory shipments to provide assistance to regions who need time to build their donor recruitment programs toward the goal of self-sufficiency.

The Clearinghouse has a national office (relocated from Irwin Memorial Blood Bank, San Francisco, CA, to AABB National Headquarters, Arlington, VA, in June 1984) which oversees five

districts/regions covering the whole United States. Requests are first referred to the regional offices, and only referred to the national office if the region is unable to comply with the request. The 1984 American Association of Blood Banks budget allocates \$459,000 for operation of the Clearinghouse, including \$39,000 for the move of the national office (21).

In addition to coordinating the movement of blood and blood components, the Clearinghouse transfers credits for blood donation between blood banks and between regions where such programs exist. Individuals giving blood in one region may receive credit for their donation in another area of the country, thereby canceling nonreplacement fees for themselves or in the name of another patient. Blood banks settle their accounts in one of two ways, depending on which program they participate in. (All payments for platelets, cryoprecipitate, and fresh-frozen plasma are handled on a cash basis; replacement fees only apply to whole blood or red cells.)

Members of the Blood Replacement Exchange may settle a debit balance by paying a \$15 replacement fee per debit or by shipping the appropriate unit(s) of blood. Centers choosing to settle via actual blood shipments also receive \$30 compensation per unit from the receiving center for processing expenses, raised from \$25 in January 1984 by AABB Board of Directors, effective in May 1984. Conversely, centers with blood credit balances either receive cash compensation (at \$15 per credit) or replacement blood shipments (and pay the \$30 processing fee). Blood replacement shipments must be type-specific and in the same type proportion as the general population. An approximately equal number of credit balances are settled by replacement blood shipments and cash payments.

Participants in the Blood Cooperative Program may outlet and receive blood and blood components on a fee-only basis (as opposed to maintaining a debit/credit balance sheet) to or from any member of the Clearinghouse. Accounts are settled monthly based on the net total of fees owed. Cooperative banks do not exchange blood credits, but may make a replacement shipment or remit the \$15 replacement fee in the name of a specific patient. (Members of the Replacement Ex-

change Program may accept blood or credit on behalf of a specific patient, but they may not ship blood in the name of a patient, as the mechanism already exists to transfer credit) (16).

In both the Blood Cooperative and Replacement Exchange Programs, blood banks are charged or credited for blood receipt or shipment according to a standard fee schedule set by the AABB Board of Directors. Cooperative members are charged a straight monetary fee according to the applicable fee schedule, while Exchange members are charged/credited according to the current breakdown between replacement and service fees. The Clearinghouse fee schedule covering inventory shipments effective January 1984 is provided in table 35.

In 1983, 47 percent of the transactions coordinated by the Clearinghouse were for actual shipments of blood or blood components. The remaining transactions consisted of issuing and/or transferring blood credits (25 percent) and payment of nonreplacement fees (28 percent). The relative proportions of the different types of transactions have changed very little in recent years [table 36]. Similarly, the volume of blood moved through the Clearinghouse has changed very little over the years, with the most noticeable change occurring in 1977, after the withdrawal of the Red Cross from the Clearinghouse [table 37].

**Table 35.—Resource Sharing Inventory Shipment Fees**

	Shipment to a cooperative bank	Shipment to an exchange bank
	Unit fee	Replacement Service fee fee
Whole blood and red blood cells. . . . .	\$40.00	\$15.00 + \$25.00
Washed and frozen red blood cells. . . . .	\$65.00	\$15.00 + \$50.00
Deglycerolized red blood cells . . . . .	\$90.00	\$15.00 + \$75.00
Platelets, cryoprecipitate, or fresh-frozen plasma . .	\$20.00	\$20.00

NOTE: The fee and replacement ratio for other components shipped under the Blood Replacement Exchange are based on mutual agreement between the shipping and receiving blood banks.

SOURCE: AABB, *Guide for the National Clearinghouse Lifeline Program of the American Association of Blood Banks*, July 1964.

**Table 36.—AABB Clearinghouse Transactions by Type**

Year	Blood	Shit) merits	Replacement fees	Credits
1983 . . . .		47%0	280/o	250/o
1982 . . . .		41	28	31
1981 . . . .		38	28	33
1980 . . . .		42	24	33
1979 . . . .		36	25	33
1978 . . . .		33	30	37
1977 . . . .		34	29	3a
1976 <sup>a</sup> . . .		35	13	52
1975 . . . .		33	13	54
1974 . . . .		28	12	47
1973 . . . .		32	11	56

<sup>a</sup>In late 1976, the American Red Cross withdrew from the Clearinghouse.

SOURCE: AABB Clearinghouse Transaction Reports, 1973-63.

## American Red Cross

In addition to the AABB Clearinghouse program, which is available to any user or provider of blood, the Red Cross has its own "Compass" system for resource sharing. Based on past surpluses or shortages, and predictions for future demand, the American Red Cross annually coordinates the exchange of blood between its regions on a contractual basis. The majority of the Red Cross sharing is internal; i.e., between Red Cross regional centers. In addition to contracted exchanges, the Red Cross arranges some sharing on an ad hoc basis, some with blood banks outside of the Red Cross.

Each Red Cross region contracts to buy from or sell to a given center a certain amount of blood on a weekly basis. That blood is committed to the contracted recipient (after the needs of the collecting region are met). Although all contracts are reported and monitored by the American Red Cross Blood Services headquarters, many agreements are initiated and completed directly between the regional centers, without the intervention or assistance of the national office.

For the 1983-84 fiscal year, the Red Cross had contracts with 33 regions for the provision of 6,729 units on a weekly basis (349,908 units annually) to 31 different recipients, both Red Cross regional centers and non-Red Cross blood banks, at a total estimated value of \$14.2 million (based

**Table 37.—Utilization of AABB Clearinghouse, 1973-83**

Year	Shipments of blood and blood components	Percent change previous year	Total transactions	Percent change previous year
1983 .....	278,032 units	+31 .60/0	587,679	+ 15.0%
1982 .....	211,296	+22.5	510,853	+ 13.7
1981 .....	172,426	- 15.9	449,397	- 8.0
1980 .....	205,263	+21 .0	488,300	+ 4.8
1979 .....	169,668	+ 2.3	466,074	- 5.8
1978 .....	165,905	-11 .7	494,982	-10.6
1977 .....	187,930	-28.2	553,859	-25.6
1976 .....	261,696	+11.6	744,583	+ 4.9
1975 .....	234,448	+19.5	709,571	+15.2
1974 .....	196,176	- 5.0	615,915	- 4.5
1973 .....	206,536	—	617,779	—

NOTE: Total number of transactions includes both the Exchange and Cooperative Programs; transactions include shipment of blood (both inventory and replacement), issue of blood credits, payment of nonreplacement fees, and returns (under 1 percent annually)

SOURCE: AABB Clearinghouse Transaction Reports, 1973-83.

on the contracted weekly volume and the fee schedule for whole blood provided by each supplying region). Of the total contracted blood supply, approximately 65 percent, or 4,344 units per week (225,888 units annually at an estimated value of \$9.25 million), are committed to 10 other Red Cross regions. Thirty-five percent (124,000 units annually) will be provided to 21 non-Red Cross blood banks.

In addition to the weekly contracts, 20 centers had an additional weekly surplus estimated at 1,500 to 1,700 units, and 5 regions had consistent surpluses (approximately 500 units/week) for which they desired exportation contracts. Both types of noncontracted weekly surpluses amount to approximately 100,000 units annually. These noncontracted surpluses are provided on an ad hoc basis.

Red Cross regional centers report any daily surpluses or shortages to the national headquarters of the American Red Cross Blood Services. If a region needs blood, the American Red Cross will match up a request with a surplus. However, regional centers often know from experience who might have a surplus and will contact another center directly. All blood exchanged through the resource sharing plan is shipped prepaid. All blood is provided at the cost of the processing and no credits for donation or blood replacement are given or exchanged. All fees are paid directly between blood centers; the American Red Cross does not handle any billing or paperwork for exchanges of blood or blood components.

The vast majority of blood or blood components moved through Compass is whole blood or red blood cells, although there is some movement of fresh-frozen plasma and cryoprecipitate, and an increasing demand for platelets. Through both the contracted and ad hoc arrangements, 71,682 units of whole blood, 469,640 units of red blood cells, 43,885 units of platelets, 21,728 units of fresh frozen plasma and 91,805 units of cryoprecipitate were actually moved in 1982-1983 (table 38). These amounts represented a decrease of 3 percent from the 1981-82 movement.

### Volume of Sharing

In describing the movement of blood in this country, it is useful to know what proportion of the total blood supply is involved. In 1980, 17.1 million units of blood or blood components were produced in the United States (518). In that year, the AABB Clearinghouse coordinated the movement of 205,263 units of blood or blood components, while the American Red Cross moved 445,433 units, yielding a total of 650,696 units, or 3.8 percent of the total available supply. This percentage represents only those units that were moved through the formal mechanisms of one of the two systems. It is impossible to estimate how much blood is moved on a local level, or through informal networking, locally or long distance. Judging from the existence and expansion of local clearinghouses such as the Metropolitan Washington Blood Banks, and the success of temporary programs such as the informal network of sup-

**Table 38.—Blood and Blood Components Moved by American Red Cross Regional Blood Centers in 1982 and 1983**

	Moved in 1983	Moved in 1982	Increase
Whole blood:			
to other RC centers. . . . .	21,653	45,763	-53%
to blood banks . . . . .	50,029	73,021	-31 %/0
Total . . . . .	71,682	118,784	-40%
Red blood cells:			
to other RC centers. . . . .	318,365	307,992	+ 3 %
to blood banks . . . . .	151,275	137,051	+ 10 %/0
Total . . . . .	469,640	445,043	+ 60/0
Platelets:			
to other Recenters. . . . .	24,493	21,742	+13%
to blood banks . . . . .	19,392	19,018	+ 2 %
Total . . . . .	43,885	40,760	+18%
Fresh-frozen plasma:			
to other Recenters. . . . .	6,029	8,537	-30%
to blood banks . . . . .	15,699	18,334	-14%
Total . . . . .	21,728	26,871	-19%
Cryoprecipitated AHF:			
to other Recenters. . . . .	74,313	67,068	+11%
to blood banks . . . . .	17,492	21,995	-20%
Total . . . . .	91,805	89,063	+ 3%
All blood and blood components:			
to other Recenters.. . . .	444,853 units	451,102 units	- 1 %
to blood banks . . . . .	253,887	269,419	- 6%
Total . . . . .	698,740	720,521	- 3%

SOURCE: American Red Cross Blood Services Operating Reports, 1982 and 1983.

port for the South Florida Blood Service, it appears that there is a substantial amount of blood which moves "off the record."

In addition, the charging and payment of non-replacement fees, and the issue and exchange of blood credits, continue at a strong rate. In 1983, over half of the Clearinghouse transactions were for the exchange or issue of credits (25 percent) or for the payment of nonreplacement fees (28 percent). While the individual responsibility philosophy is not universally accepted, it is still widely used in this country.

The figures of the American Red Cross for the past 5 years indicate an absolute increase in the amount of blood and blood components which were produced but fail to suggest a trend toward or away from increased blood movement (table 39). The lack of a pronounced increase in the percentage of blood moved denies a widening gap between surplus and shortage areas. Similarly, the net volume of blood and blood components moved through the AABB and the ARC has continued to rise (table 40), although the pattern

**Table 39.—Movement of Blood and Components Through the American Red Cross, 1979-83**

Year	Volume moved through ARC	Total production by ARC	Percent total production moved
1983 . . . . .	698,740 units	14,331,858 units	4.9%
1982, . . . . .	720,521	13,045,189	5.5
1981 . . . . .	562,431	12,052,017	4.7
1980, . . . . .	445,433	11,233,274	4.0
"1979 . . . . .	332,971	10,465,129	3.2

SOURCE: American Red Cross Blood Services Operating Reports, 1980-83,

seems to reflect the influence of variables such as the change in number of members in the Clearinghouse, and the amount of sharing arranged outside of either formal network, rather than an increasing demand for imported blood within deficient regions.

## Conclusion

The blood collection organizations are largely in agreement about the need for resource sharing. The current lack of cooperation between the AABB and the Red Cross appears to be due to concerns about antitrust violations. There is lit-

Table 40.—Total Movement of Blood and Blood Components in the United States, 1979-83 (including both the **AABB** and the American Red Cross)

Year	Clearinghouse	Red Cross	Total	Percent change from previous year
1983 . . . . .	278,032 units	698,740 units	976,772 units	+ 4.80/o
1982 . . . . .	211,296	720,521	931,817	+26.8
1981 . . . . .	172,426	562,431	734,857	+ 12.9
1980 . . . . .	205,263	445,433	650,696	+29.5
1979 . . . . .	169,668	332,971	502,639	NA

SOURCE AABB Clearinghouse Transaction Reports, 1979-83; and American Red Cross Blood Services' Operating Reports, 1980-83.

tle evidence to support the notion that the Red Cross, or any of the other blood collecting organizations, sought to block the most recent resource sharing agreement in hopes of retaining organizational control over its blood supply. Concerns about nonreplacement fees remain to a lesser extent but are superseded by concerns for a well-managed blood supply. The nonreplacement fee continues to be supported for recruitment reasons in selected areas of the country; in other areas, the fee is adamantly opposed. The trend, however, is away from the nonreplacement fee, and it will likely become a nonissue in terms of logistics and sharing of blood resources. The philosophical objections to cooperating with organizations operating under different recruitment strategies have subsided.

Even without a single coherent national sharing system or the implementation of the Resource Sharing Agreement (the one attempt at formalized resource sharing between the major organizations in the voluntary sector: the AABB, ABC, CCBC and the ARC), regions with blood shortages are generally able to meet their needs, either through long-term contracts for blood provision or ad hoc arrangements to compensate for unexpected demand or shortages. Individual blood centers often contract with other blood centers outside of the formal mechanisms of the Clearinghouse or the

Red Cross, as well as within them. For instance, in 1983, the South Florida Blood Service received 70 percent of its imported blood through long-term contracts, 21 percent through ad hoc arrangements, and only 9 percent through the formal mechanisms of the Clearinghouse.

Contrary to the situation in past years, the supply of blood in the United States is no longer a critical concern. Blood is managed and shared effectively, as witnessed by low outdate rates and consistent interregional movement of blood. Efforts at coordination by the private sector have been largely successful.

On the local level, many areas have coordinated their blood services, either through the ABC Regionalization Program or through individualized approaches. In the remaining areas, discussion has at least been initiated on the means for regional coordination. Nationally, the two voluntary sharing systems provide an effective means for moving blood from "place of plenty" to "place of need." In addition, blood bankers are predisposed toward assisting in times of blood supply emergencies and temporary shortages, so many ad hoc arrangements are made between individual blood service facilities. Thus, the combination of formal and informal sharing works, though it might be more efficient in individual instances.

### PART 3: IMPACT OF HEALTH CARE COST CONTAINMENT

The rising cost of health care has been a persistent and growing problem for a number of years. In the past several years, a number of cost containment efforts have been adopted; for ex-

ample, greater use of health maintenance organizations and home health care services and more extensive coinsurance requirements. Perhaps the most far-reaching effort at health care cost con-

tainment was Medicare's introduction in October 1983 of a new system for hospital reimbursement based on a prospective per-case payment using diagnosis-related groups (DRGs). Under this form of payment, hospitals will be paid a specific amount for each patient treated in a particular group, regardless of the number or types of services provided.

Until October 1983, Medicare employed a retrospective cost-based reimbursement approach whereby hospitals could recover from Medicare most of what they spent for Medicare beneficiaries. Any costs incurred in treating Medicare patients, including costs of blood products, were effectively "passed through" to Medicare (or to patients and any other insurance they may have had). Similar cost-based reimbursement systems covered many non-Medicare patients. There was little incentive for hospitals to control costs. Under the new system, however, hospitals will be rewarded for reducing the cost of treating a patient over the entire course of the hospital stay. The new system is likely to have an effect that reaches far beyond the Medicare system if it is adopted by other third-party payers. Per-case payment encourages the hospital and its physicians to consider explicitly the benefits of any services against their added costs. Thus, Medicare's prospective payment system is likely to affect all health care suppliers, including the blood services complex.

Per-case payment systems such as DRGs provide a number of incentives to hospitals which are not present under cost-based systems. Two general incentives to hospitals in any per-case payment system are: 1) to reduce the cost to hospitals of each inpatient stay, and 2) to increase the number of inpatient admissions. Cost per case can be reduced by decreasing the number of inpatient days, but it can also be reduced by using fewer technological services or attempting to provide them at lower cost. In addition, because outpatient care is excluded from the current DRG system, hospitals may be encouraged to arrange to provide more services, including ancillary services, on an outpatient basis. Finally, hospitals may seek to increase profitable admissions by manipulating case load.

The direction and strength of these incentives for any particular hospital will be altered by key features of the DRG payment system (e.g., the proportion of the hospital's case load covered by DRG payment, the treatment of costs as pass-throughs), as well as by other system constraints (e.g., physicians' incentives to practice high-quality medicine, community pressure to provide certain services), so that specific outcomes of implementing the DRG system for any part of the health care system, including blood services, are difficult to predict.

One result of hospital efforts to contain costs that is already being felt by some blood suppliers is a tendency for transfusion services to "shop around" for blood products. Although there are some indications of product preference (e.g., 308), the safety and efficacy of blood products are for the most part standardized. Thus, the only factors differentiating blood products are cost and availability. As shown in chapter 3, fees for blood services vary widely among blood suppliers; thus, it is possible for blood users to compare costs. The use of preservative systems for blood components, and the computerized communications systems now in place, make availability less of a problem, except perhaps for components with short shelf lives, such as platelets.

Assuming that availability needs can be met, comparative shopping may lead to increased use of the AABB Clearinghouse, greater price competition among blood suppliers, and a breakdown of regionalization programs (383). At a minimum, competition should result in more contract negotiation between blood suppliers and transfusion services. In the long run, the result could be either lower prices across the Nation or more negotiation about prices among blood suppliers—resulting, perhaps, in a standard price for blood products. DRGs may have little effect on the plasma derivatives market, which is already highly competitive (see ch. 3).

One manifestation of hospitals' comparative shopping on the basis of price may be increasing questioning of the cost structure of blood suppliers' processing fees. As discussed in chapter 3, blood suppliers have not devised a uniform in-

dustrywide system to account for the costs of their blood products. Blood suppliers have recently experienced steady increases in the excess of revenues over expenses, often attributing such increases to needs for capital expansion or research. Where competition is not a viable option, hospitals may exert pressure on blood suppliers to bring down costs by limiting or seeking other avenues for funding research projects or capital expansion. Demands for price concessions may have particular adverse effects on independent (i.e., non-Red Cross) blood centers which have built part of their reputations on research.

DRGs are most likely to have the effect of revitalizing hospital transfusion and pharmacy committees' monitoring of physicians' use of blood products. This effect may not be limited to the whole blood sector. In general, hospital utilization reviews and quality audits are likely to increase under DRGs (550). As discussed in part 4 of this chapter, the appropriate use of blood products has been a topic of concern, primarily because of safety considerations, but sometimes (e.g., albumin), for reasons of cost. The implementation of DRGs will give hospitals both an added incentive to monitor individual physicians' use of blood products and a systematic means for monitoring hospitalwide use. The implementation of DRGs is expected to increase the reliability of patient discharge data, because payment will rely on the accuracy and timeliness of discharge abstracts (550). It will also provide a systematic way to match blood use to specific diagnoses, an area in which national blood data are particularly lacking.

Methods to correlate patient outcome with aspects of hospital care are also being devised (551), and these may be useful for studies of efficacy of blood components. Studies of the relationships between use and patient outcome will be important because utilization reviews have often focused on cost containment to the exclusion of concerns about quality of care (545), although such studies will add to administrative costs.

The cost of blood products may come to affect hospitals' case mix, and as a result, blood suppliers' production schedules. There is speculation

that for certain patients (e.g., post-heart surgery, post-vascular surgery, oncology patients), DRG allocations may be depleted on blood demands alone (see, e.g., 12). For example, in a bleeding patient the cost of platelet concentrates alone may be as high as \$360 for 1 day. Under the DRG system, hospitals may become more specialized in their care, treating only certain groups of patients. Presumably, the rise of specialized care centers will make for more rational adjustments in per-case reimbursement rates, rather than affecting patient access to care—although this may be a short-term effect. Patients may have to travel farther to specialized care centers.

The net long-term effect of these changes may benefit patients, assuming the appropriate adjustments in DRG reimbursement rates are made so that specialized care hospitals are not adversely affected by serving large-volume blood users. Recent research has shown that patients treated in hospitals serving large numbers of specific diagnoses have better outcomes (188). Blood suppliers, however, may have to adjust collection and production schedules as client hospitals change their case load mix. For example, regions with transplant centers may require increased donations.

It is difficult to determine whether DRGs will affect the present balance between hospital blood bank and community blood center collections. Community blood centers have come to dominate blood collections (see ch. 3). There is speculation, however, that hospitals may set up their own donor rooms in an attempt to contain and control costs of blood services. Although the question of economies of scale in community blood centers remains open, it is doubtful whether hospitals would enjoy any economies of scale from collecting and processing their own blood products. For example, Wallace and Wallace/ABC (576) found that collecting hospitals charged more for blood (although it is difficult to determine whether higher charges actually reflected higher costs of collection).

Small-volume hospitals would find it particularly difficult to maintain the necessary levels of expertise in donor recruitment, collection, and processing, in addition to being unable to make

the necessary space available. What may happen is that a selected number of highly specialized hospitals may begin to provide for their own special needs (e.g., for platelets and granulocytes from pheresis; see 372). Because outpatient services do not currently come under DRG regulations, DRGs may temporarily favor transfusion services that are independent blood centers. For example, all Red Cross blood services have applied for Medicare provider certification.

The extent to which blood centers will be able to be reimbursed as Medicare providers is limited, however. The Health Care Financing Administration (HCFA) recently rescinded the Medicare provider certification of a blood bank, noting that, "as the law now stands, a blood bank cannot be paid directly for services it renders" (412). The intermediary had originally considered the blood bank in question as eligible for direct Medicare payment on the assumption that the blood bank would be considered a physician-directed clinic. According to HCFA, under current law the blood bank is only allowed to bill for physicians whom the blood bank employs or has a contractual arrangement with, and who administer blood, but not for services rendered by paramedical personnel.

Similarly, HCFA refused to make an exception to the Medicare provision limiting therapeutic apheresis procedures to inpatient or outpatient settings (172). The blood bank in question wanted to be granted an exception on the basis that it was a physician-directed clinic. Thus, a move by blood centers to be considered comparable with outpatient units and increase their service base, as well as help hospitals take advantage of anomalies in the current reimbursement system, may meet resistance from HCFA. It is expected that eventually outpatient care will also be covered by a prospective payment system.

Multi-hospital chains, both profit and non-profit, are another response to government scru-

tiny of health care costs. Such chains are believed to provide more efficient management (98). There was some speculation that multi-hospital chains might find it in their interest to take over functions such as blood services, but apparently blood services were not considered profitable enough to get involved in (270), and blood collection and distribution will be left to the largely not-for-profit sector.

Apart from DRGs, private efforts at cost containment may result in changes in the blood services system, such as an increase in the use of nonreplacement fees, or similar credits applicable to processing fees. Self-insurers (and participants in corporate donor programs), such as Wells Fargo Bank in California, have expressed concern that the cost of blood may be inordinately high because donors effectively subsidize nondonors (259). It may be that such corporations will request some form of credit for their employees in exchange for holding mobile collection drives.

To summarize, the effects of DRGs and other cost containment efforts are difficult to predict. A special commission has been established to monitor the effects of the DRG system and devise necessary modifications. Health care providers, including those in the blood services complex, are watching and hoping to influence developments in the Medicare reimbursement system (e.g., 24). It is unlikely that there will be a significant change in the organizational structure of blood collections—i.e., blood center collections should continue to predominate and perhaps increase their influence. However, hospitals may exert pressure on blood collectors to reduce charges for blood products, and blood centers in some areas may have to change their product mix. The greatest impact of DRGs may be on the ability of independent blood centers to conduct research and expand their facilities. DRGs will certainly provide an opportunity for more stringent monitoring of blood product utilization.



## PART 4: APPROPRIATE USE OF BLOOD PRODUCTS

### Introduction

Both blood suppliers and users agree that blood is overused and used inappropriately, but they differ about the extent to which it is misused and about the means to promote more appropriate use. Estimates of the amount of blood products which are inappropriately used are high: 20 to 25 percent for red cells (204); up to 90 percent for albumin (8); and 95 percent for fresh-frozen plasma (457). However, data by which to evaluate the overall appropriate use of blood products do not exist, in many cases because of lack of scientific precision concerning when a component or derivative should be administered.

In addition, while some data exist on the number of patients transfused with particular blood products (e.g., 518), national data on the reasons why transfusions were given are harder to come by. Studies such as Friedman's (204) of the diagnostic categories for which red cells were transfused (as well as the relationship between such transfusions and geographic location, patient age and gender) have not been conducted for other blood products.

Perhaps as important as overall trends in the use of blood products are instances of bad transfusion practice which are believed to occur (19). As with appropriate use, national data on the extent of such bad practices do not exist.

What is known is that there are wide geographic variations in the rate of transfusions. For example, transfusion rates for red cells and whole blood varied from a high of 15.3 patients per thousand population in the Mid-Atlantic States to 12.9 per thousand population in the Mountain States. Hospitals in the New England region transfused 50 units of red cells per thousand population, compared to only 36 units per thousand population in the Mountain States (518). The reasons for these variations are not known. Although general guidelines exist (e.g., 17), in many cases transfusion decisions, like many other medical decisions, rely on clinical judgment. In addition, handbooks widely used by physicians (e.g., 425) may contain information which is inconsistent

with guidelines written by experts in transfusion. There are wide variations across the United States in other areas of medical practice, such as lengths of hospital stays, that are not adequately explained by demographic differences or differences in health outcomes (553).

Concerns over misuse have focused on different blood products over time. Initially, questions centered on the widespread practice of infusing whole blood instead of packed red cells. Current questions involve albumin solutions, fresh-frozen and single-donor plasma. For example, a National Institutes of Health Consensus Development Workshop on fresh-frozen plasma indications and risks was held in September 1984.

### Whole Blood

Whole blood transfusions decreased from 67.4 percent of total blood component transfusions in 1971 to 13.0 percent in 1980, and from 78 percent of transfusions involving red cells to 19 percent (see fig. 6 in ch. 3). More recent nationwide information on transfusions is not available, but Red Cross data indicate that production of units of whole blood continues to decrease: by 12.2 percent between 1980 and 1981; by 11.6 percent between 1981 and 1982, and by 20.7 percent between 1982 and 1983. For the year ended June 30, 1983, only 893,791 units of whole blood were produced in the Red Cross system, compared to 5,328,403 units of red cells.

In addition to the normal range of transfusion hazards, risks specific to the use of whole blood are circulatory overload as a result of rapid and excessive infusion, and immunization to platelets and granulocytes. Circulatory overload can result in pulmonary edema and congestive heart failure, especially in patients whose cardiovascular status is precarious or compromised (273,388). Transfusions of whole blood are also viewed as not cost effective. Two or more components can be made from every unit of whole blood. Recovered or salvaged plasma can be sold by the blood center for additional revenue.

For some physicians, the only valid indication for the use of whole blood is when a patient needs blood, but are without some of its dangers. Risk of circulatory overload is reduced, as are risks of red blood cells and plasma simultaneously; i.e., citrate and ammonia intoxication; metabolic acidosis; acid/base imbalance; and some forms of allergic and febrile reactions (369). Another important clinical advantage of red cell concentrates (407, 500). Others (e.g., 395) see no need for either fresh or stored whole blood in clinical practice, and believe that all use of whole blood should be replaced by a "three-tiered" combination of: 1) volume expansion with a fluid; 2) red blood cell replacement; and 3) the risk of infusion of large amounts of donor replacement of clotting factors, if necessary.

There are also different guidelines on the percentage of blood loss indicative of transfusion with either whole blood or a combination of other components (e.g., 17,500); the type of fluid replacement to use if whole blood is not used (see discussion of albumin below); and the amount of whole blood to transfuse, in particular the requirement for a single unit of whole blood (e.g., 202,369).

Use of red cell concentrates has been found to vary considerably by geographic location, age, store volume and oxygen-carrying capacity, gender, operative status (i.e., operated v. non-operated), diagnostic category, and even by appropriately when used to provide "general support" to treat hypoproteinemia with some degree of anemia (see 202,203,204; and, for a more limited analysis, 518). In studies of 1974 of concomitant anemia, or to prepare a nutrient-deficient patient for some form of stress treatment. According to one textbook of transfusion medicine, the latter represent "serious misconceptions about the efficacy of blood transfusion, except one, males received a higher mean amount of units.

Not surprisingly, surgical patients were transfused more often than nonoperated patients, and older patients more than younger patients. Patients over 65 years of age constituted 44.3 percent of transfused patients, and received 43.7 percent of all units transfused (204). The major mistake was that whole blood stored over 24 hours contains few viable platelets and granulocytes, and transfused in Friedman's study of 1977 data were levels of Factors V and VIII are reduced (17).

## Red Cell Concentrates

Red cell concentrates are seen as preferable to whole blood in many instances, because red cells have the same oxygen-carrying capacity as whole blood, but are without some of its dangers. Risk of circulatory overload is reduced, as are risks of red blood cells and plasma simultaneously; i.e., citrate and ammonia intoxication; metabolic acidosis; acid/base imbalance; and some forms of allergic and febrile reactions (369). Another important clinical advantage of red cell concentrates (407, 500). Others (e.g., 395) see no need for either fresh or stored whole blood in clinical practice, and believe that all use of whole blood should be replaced by a "three-tiered" combination of: 1) volume expansion with a fluid; 2) red blood cell replacement; and 3) the risk of infusion of large amounts of donor replacement of clotting factors, if necessary.

**Table 41.—Blood Utilization by Major Disease Categories Ranked by Total Units Transfused and Percent of Units Transfused: Operated Males, Nonoperated Males, Operated Females, Nonoperated Females, and All Patients in Each Category**

Major disease category	Operated males			Nonoperated males			Operated females			Nonoperated females			All patients		
	Total units transfused	% of units transfused all patients	% of units transfused to all patients	Total units transfused	% of units transfused all patients	% of units transfused to all patients	Total units transfused	% of units transfused all patients	% of units transfused to all patients	Total units transfused	% of units transfused all patients	% of units transfused to all patients	Total units transfused	% of units transfused all patients	% of units transfused to all patients
1. Malignant neoplasm	0,166	5.7	3.8	6,687	3.8	5.4	9,570	5.4	6,728	3.8	33,097	18.7			
2. Cardiovascular disease including cerebrovascular disease	4,957	4	6	2,792	6	4	7,277	4	3,678	2.1	28,644	16.1			
3. Nonmalignant disease of the gastrointestinal tract	5,807	3.3	5.0	8,947	5.0	3.1	5,475	3.1	7,607	4.3	27,776	15.7			
4. Fractures and traumatic injury including soft tissue injury	9,946	5.6	0.5	889	0.5	5.4	9,570	5.4	892	0.4	21,298	12.0			
5. Anemia including acute hemorrhagic, hemophilia, and other diseases of the hematopoietic system	447	0.3	1.9	3,383	1.9	0.4	673	0.4	4,750	2.7	9,253	5.2			
6. Obstetrical procedures and complications	0	0	0	0	0	3.6	6,392	3.6	1,289	0.7	7,681	4.3			
7. Bone and joint disease excluding fracture	2,134	1.2	0.1	157	0.1	1.9	3,421	1.9	423	0.2	6,135	3.5			
8. Disease of respiratory tract and lungs	1,386	0.8	0.9	605	0.9	0.4	776	0.4	1,275	0.7	5,042	2.8			
9. Liver disease, portal hypertension, and esophageal varices	352	0.8	1.0	1,692	1.0	0.3	579	0.3	234	0.7	4,797	2.7			
10. Disease of the kidney, urinary bladder, and urethra	1,501	0.8	0.5	882	0.5	0.8	1,389	0.8	953	0.5	4,725	2.7			
11. Nonmalignant gynecologic disease including uterine leiomyomas and breast disease	8	0.005	0	0	0	2.4	4,230	2.4	416	0.2	4,654	2.6			
12. Complications of surgery and medical care	1,171	0.7	0.1	200	0.1	0.7	1,276	0.7	201	0.1	2,848	1.6			
13. Perinatal conditions	497	0.3	0.6	002	0.6	0.2	348	0.2	854	0.5	2,701	1.5			
14. Benign tumors excluding uterine leiomyomas	390	0.2	0.01	16	0.01	1.2	2,164	1.2	116	0.1	2,686	1.5			
15. Gall bladder and bile duct disease	778	0.4	0.04	72	0.04	0.7	1,207	0.7	109	0.1	2,166	1.2			
16. Disease of prostate gland and other male genital organs	925	1.1	0.1	125	0.1	0	0	0	0	0	2,050	1.2			
17. Nutritional, congenital, and metabolic disease	670	0.4	0.1	151	0.1	0.4	691	0.4	237	0.1	1,749	1.0			
18. Disease of skin, soft tissue, connective tissue and muscle, excluding traumatic injury	436	0.2	0.1	124	0.1	0.4	670	0.4	269	0.2	1,499	0.8			
19. Infectious disease including viral hepatitis	257	0.1	0.3	455	0.3	0.2	307	0.2	377	0.2	1,396	0.8			
20. Hernias	505	0.3	0.1	106	0.1	0.2	397	0.2	168	0.1	1,176	0.7			
21. Diabetes mellitus including complications	300	0.2	0.1	122	0.1	0.2	414	0.2	299	0.2	1,135	0.6			
22. Disease of the pancreas	352	0.2	0.1	138	0.1	0.1	173	0.1	112	0.1	775	0.4			
23. Disorders of central and peripheral nervous system excluding vascular and psychiatric disease	61	0.1	0	2	0	0.1	85	0.1	199	0.1	657	0.4			
24. Disorders of fluid, electrolyte, and acid-base balance	25	0.01	0.1	127	0.1	0.03	59	0.03	190	0.1	401	0.2			
25. Disease of endocrine glands other than pancreas	135	0.1	0.02	27	0.02	0.04	69	0.04	82	0.05	313	0.2			
26. Disease of	22	0.01	0.03	52	0.03	0.02	38	0.02	59	0.03	171	0.1			
Totals (this table)	55,328	31.2	16.8	29,863	16.8	32.2	57,116	32.2	32,517	18.3	174,824	98.5			
Miscellaneous (no category assigned)	368	0.2	0.4	724	0.4	0.3	529	0.3	953	0.5	2,574	1.5			
Totals (all patients)	55,696	31.4	17.2	30,587	17.2	32.5	57,645	32.5	33,470	18.9	177,398	100.0			

SOURCE: B. A. Friedman, I. L. Burns, and M. A. Schork, *A Study of National Trends in Transfusion Practice*, 1980.

Stored red cells, whether packed or in whole blood, do not contain functional platelets or granulocytes. However, the nonfunctional platelets and granulocytes contained in red cell concentrates (and whole blood) can result in alloimmunization. Thus, for patients who have already indicated reactions to transfusions—in particular, urticarial reactions—or for patients likely to be receiving frequent transfusions, washed or, less frequently, frozen-thawed-deglycerolized red cells are indicated (17). These prepared components are 1.5 to 3.5 times as expensive as unprocessed red cells. They account for very little of total red cell production. In the Red Cross only 46,802 units of frozen red cells and 50,952 units of washed red cells were produced in 1983.

A major textbook of transfusion medicine notes that: “Despite a large and longstanding experience, the indications for transfusion of red blood cell products are not always easy to delineate. ” There is a wide variety of available transfusion products, wide variation in the homeostatic capabilities of patients, and a multiplicity of clinical situations. Thus, while providing some general principles, the textbook suggests that “rules of thumb about when to transfuse, optimal hematocrit levels, and other such notions are unrealistic” (407). Others (e.g., 201) suggest that more objective clinical criteria for blood transfusion can and should be developed.

One of the most controversial areas concerning red cells is the matter of the “transfusion trigger,” or the hemoglobin level which indicates to physicians that a patient will be injured by oxygen deprivation, requiring a transfusion of red cells. Patients vary considerably in their tolerance of anemia. For example, women naturally have lower hematocrits than men, but surgeons appear to use the same support and ceiling hematocrit levels to regulate blood transfusion for both genders (202). Similar practices exist for patients in diagnostic categories such as chronic renal failure and chronic obstructive pulmonary disease (232). A hemoglobin of less than 10 g/all has been the traditional “transfusion trigger” most often used by physicians (204).

Recently, alternatives have been suggested. While clinical judgment of the patient’s condition is suggested most often (e.g., 17,407), Gould (232) sug-

gests combining clinical status with an evaluation of a patient’s ratio of oxygen consumption to oxygen delivery (“oxygen extraction ratio” or ER) rather than a hemoglobin count,

Red cells are sometimes used instead of a more appropriate nonblood therapy. For example, Friedman and his associates found that iron deficiency anemia was the fifth leading blood-user diagnosis group in the United States among non-surgical patients (204). This condition rarely warrants blood transfusion (201). Rather, it is treatable with dietary change or iron supplements.

## Platelets

Patients most likely to require platelet transfusions are those suffering from malignancies involving the bone marrow (e. g., leukemia and lymphoma), those suffering from bone marrow depression as a result of chemotherapy, drugs, infection or other causes (e. g., 481), and those suffering from drug-induced thrombocytopenia (platelet loss). Deaths due to leukemia have significantly declined since the introduction of platelet therapy. Surgical patients suffering from thrombocytopenia may also require platelet transfusions (199,533).

The risk of hepatitis and other transmissible infectious diseases from platelets is the same as for whole blood. As with whole blood transfusions, circulatory overload can occur, especially in children. In addition, because platelets are stored at room temperature, the risk of bacterial growth is greater than that of whole blood. Risks specific to random-donor platelet transfusions include alloimmunization resulting in a refractory state, transfusion reactions as a result of incompatibility between antibodies in the platelet concentrate and red blood cell antigens of the recipient, and graft v. host disease as a result of the collection of lymphocytes along with the platelets. When sensitivities develop, single-donor transfusions are substituted for random-donor platelet concentrates, although these are not without their problems (533).

It is generally recognized that there are large gaps in knowledge of the proper use of platelets (481). There is general agreement that platelet transfusions are of limited benefit in patients suf-

fering from idiopathic thrombocytopenic purpura and other forms of rapid platelet destruction (264,533). There are different opinions concerning the use of platelet transfusions when other forms of platelet dysfunction (thrombocytopathy) are present. For example, the AABB Physicians Handbook indicates that platelet transfusions are indicated for thrombocytopathy. Daly (145) indicates that such transfusions are rarely necessary.

As with other components, the proper dosage of platelets is a matter of unresolved clinical concern. Aster (55) notes that treating the “platelet count” rather than the patient may result in waste. Other questionable uses of platelets are for open heart surgery, irrespective of a patient’s own platelet level and clinical status (on the assumption that a qualitative platelet defect exists), and in patients who develop a hemorrhagic diathesis after renal transplantation (55).

Most significantly, some question the prophylactic use of platelets in patients with malignancies. Clinical trials investigating this question have led to different conclusions (481); another clinical trial is currently under way (533). The resolution of this question will have a major effect on the blood supply and economics of blood services (520).

## Granulocytes

Granulocyte transfusions maybe indicated for patients who have an inadequate supply of white cells (granulocytopenia) and a life-threatening infection which is unresponsive to antibiotics. Candidates for granulocyte transfusions include patients with acute leukemia, aplastic anemia, solid tumors and auto-immune diseases, and transplant recipients. Granulocytopenia can result from chemotherapy or primary bone marrow depression.

Granulocyte transfusions carry the same risks of infectious disease as whole blood. In addition, immunosuppressed or immunodeficient recipients may be at risk of developing graft v. host reactions. Allergic, febrile or hemolytic reactions, HLA and red cell antigen immunization, and severe pulmonary insufficiency can occur (17, 369). Granulocyte transfusions are expensive because of the complexities of cell procurement, storage and administration and the requirement for

close day-to-day cooperation between clinicians and the transfusion service. For example, granulocytes must be obtained, crosshatched, and administered within 24 hours of donation, putting enormous pressure on blood banks and transfusion services. Granulocyte donors may be particularly at risk because granulocytes must be obtained via pheresis and alloimmunized patients may rely on a small pool of donors.

Indications for use of granulocytes are perhaps the least clear of all the components, with the exception of fresh-frozen plasma (199,481). As a result of several clinical investigations, including clinical trials (e.g., 191,482,590), the prophylactic use of granulocyte transfusion has been judged to be of questionable therapeutic value, at a minimum (17). Some say the use of prophylactic granulocytes should be considered a strictly investigational procedure not to be utilized outside of research settings (e.g., 481). The therapeutic value of granulocytes has been difficult to judge because of the seriously compromised clinical status of candidates for granulocyte transfusions (e.g., 190). The use of granulocyte transfusions has been declining nationwide. In general their use to combat infections seems to be a therapy of last resort.

## Cryoprecipitate

Cryoprecipitate contains large amounts of Factor VIII and von Willebrand’s factor, in addition to concentrated amounts of fibrinogen, fibronectin, and Factor XIII. The major clinical disadvantage of cryoprecipitate is the individual variation in Factor VIII from bag to bag, resulting in unpredictability of the required therapeutic dose (397). Cryoprecipitate has all the infectious risk factors of whole blood. Other risks include febrile and allergic reactions, and hemolysis as a consequence of incompatibility between antibodies in cryoprecipitated AHF and antigens of recipient red blood cells.

Indications for cryoprecipitate vary. It is recommended for the treatment of Hemophilia A and von Willebrand’s disease, congenital fibrinogen deficiency, and other conditions associated with consumption of fibrinogen (e.g., obstetrical com-

placations, disseminated intravascular coagulation) and Factor XIII deficiency (e.g., 17,282). Others do not mention Factor XIII deficiency (369). The most recent use of cryoprecipitate has been for fibronectin replacement in infection or shock. This use has been questioned, because clinical indications have not been adequately tested, and administration of excess fibronectin may be harmful to the recipient (497).

The major controversy surrounding the use of cryoprecipitate is its use in preference to lyophilized Factor VIII concentrate. Preparation of cryoprecipitate is a labor-intensive process. Administration is more difficult because, unlike lyophilized Factor VIII, cryoprecipitate must remain frozen to retain its therapeutic value. As already noted, the Factor VIII content of cryoprecipitate varies from unit to unit and is largely unknown. While the conventional wisdom is that cryoprecipitate is less likely to transmit infectious disease because fewer donors are involved, in fact a severe hemophiliac treated with cryoprecipitate would be exposed to 500 to 1,000 donors a year. If one of the units is contaminated with a low-prevalence virus, the hemophiliac receives all of it. In a commercial pool, a low-prevalence virus would be diluted and might be inactivated by antibody in the pool.

### **Fresh= Frozen and Single= Donor Plasma**

Single-donor plasma, fresh-frozen (usually called fresh-frozen plasma, or FFP) contains all the coagulation factors found in native plasma. Single-donor plasma (not frozen) contains all of the stable coagulation factors but reduced levels of the labile coagulation Factors V and VIII. Both fresh-frozen and single-donor plasma have all the risks of infectious disease that whole blood has, as well as the risk of allergic or febrile reactions and incompatibility between plasma antibodies and recipient red cell antigens. Transfusion of plasma to correct for coagulation deficiencies carries with it the risk of fluid overload (17).

The dramatic increase in the use of fresh-frozen plasma over the last decade has prompted concerns that the uses of it "are often vague and without scientific basis," and that it is "likely that other products are available that are equally effective

as and safer than fresh-frozen plasma" (567). Most FFP is administered as replacement for deficient coagulation factors in postoperative patients and in a variety of medical bleeding disorders. Some also is used as a replacement for fluid and colloid loss in patients with burns and shock. As with other components, systematic data on the purposes for which fresh-frozen plasma is used are not available.

Recommended indications for FFP and single-donor plasma vary. The most frequently cited indication for fresh-frozen plasma is the situation in which a specific factor deficiency has not been established (17,282,369,397,497). *Harrison's Principles of Internal Medicine* (425) indicates that fresh-frozen plasma ("and cryoprecipitate") is necessary for treatment of coagulation disorders, especially hemophilia, a suggestion that most experts in transfusion do not agree with. There is disagreement over the use of FFP and single donor plasma in other situations, in particular for the treatment of low plasma volume (17,282,369,397, 497). The use of other solutions for fluid replacement would obviate the risk of infectious disease.

Other indications on which there is disagreement include the use of FFP: as a protein-containing medium (282); as a source of Factor IX (282); for disseminated intravascular coagulation and when deficiencies of multiple clotting factors exist, as in liver disease (397; 497); the preparation of hemostatically deficient patients and intra- and postoperative correction of bleeding problems (497).

### **Albumin and Plasma Protein Fraction**

The primary indication for administration of albumin (and a similar product, plasma protein fraction [PPF]) is for plasma volume expansion in shock and trauma. Because albumin and PPF are heat-treated, they are safer than whole blood with respect to transmission of infectious disease. Most adverse reactions are due to technical accidents during manufacture (520) or to inappropriate or incorrect administration (494,538). Recipients of albumin run the risk of fluid overload.

Like fresh-frozen plasma today, the overuse of albumin was once a topic of great concern. Al-

though its use remains controversial (see below), public concern about the use of albumin appears to have subsided. Cost was a major element in the controversy. Albumin is considerably more expensive than crystalloid solutions such as saline and Ringer's lactate. A liter of Ringer's lactate solution costs approximately \$1; an amount of albumin required to produce a comparable result costs \$130 (394). One estimate is that as much as 10 percent of the total drug budget for an acute hospitalization may be related to use of albumin and other blood products (112).

In 1975, indications for the use of albumin were the subject of an NIH Workshop (494). Following the workshop, guidelines for the use of albumin were published (538), and a number of attempts were made to modify physicians' use of albumin (e.g., 8). As late as 1977, however, Alexander, et al. (8), found that albumin was being used inappropriately in 71 percent of surgical cases and 41 percent of nonsurgical cases. Worldwide U.S. production and consumption continues to rise (see ch. 3). A recent international study (including the United States) found that clinical uses of albumin covered many uses not recommended by health and regulatory agencies—e.g., for nephrosis, in detoxification, and as part of the treatment of malignancies (260). An indication of the confusion about the amount of albumin that is needed in clinical practice is the significant variation among countries, even countries similar in levels of medical sophistication (388).

Despite the guidelines published as a consequence of the NIH workshop, textbooks continue to disagree on some of the uses of albumin; e.g., in adult respiratory distress syndrome (17,112, 349,520) and coronary bypass pump priming (388,520). The latest edition of *Harrison's Principles of Internal Medicine* (425) cites the use of albumin in severe malnutrition, nephrosis, and certain gastroenteropathies. Use of albumin for malnutrition is not advised in manuals written by blood bankers (e.g., 17). The international study referred to above suggested that the needs of patients were reflected better by clinical use than by agency recommendations. Thus, use of albumin remains controversial.

## Factor VIII

Until the AIDS crisis, there was little controversy in this country concerning the appropriate use of Factor VIII, particularly since it is readily available. There is now some movement from use of lyophilized Factor VIII to use of cryoprecipitate, at least for less severe hemophiliacs. Use of lyophilized Factor VIII has reportedly decreased substantially in the past year. In countries where Factor VIII is less available, prophylactic use of Factor VIII is an issue. Mollison (388) reports the results of a randomized clinical trial conducted in Great Britain (54) which showed that reducing the incidence of bleeding in severe hemophiliacs by 15 percent would require the use of 73 percent more Factor VIII than would be used by simply treating episodes of bleeding. Reduction of bleeding by 66 percent would involve an increased usage of approximately 160 percent.

## Methods to Change Usage Patterns

To some extent, then, controversy surrounds the appropriate use of all blood products. A key element in the controversy is that criteria for clinical use are often unclear. Thus, practice at the bedside relies on anecdotal reports and evidence from inadequate trials (567). However, even when medical guidelines are generally accepted, local practice varies and may sometimes be inappropriate. Past attempts to change medical practice have relied largely on educational efforts. Although systematic data do not exist to adequately test their effectiveness, these attempts appear to have been largely unsuccessful. Currently, a number of new efforts to curb the misuse of blood products, described below, are under way. Perhaps the most effective push in the direction of more appropriate use will be the impact of Federal cost containment efforts.

## Education

As noted above, past attempts to change medical practice have relied largely on educational efforts such as seminars and textbooks. For example, the American Association of Blood Banks has published a series of books based on seminars and

workshops at their annual conventions. Three textbooks are available (Huestis, Bove, and Busch [three editions]; Petz and Swisher, 1981; and, Mollison [seven editions 1951-83]). It is unclear, however, to what extent these efforts have reached practicing physicians. Medical schools devote little attention to transfusion practice. The result is that medical students and residents learn most of what they know about blood transfusion by the practice of "chaining" (520): "The chief resident passes along what he has learned, gathered in an entirely unsystematic way, to the assistant residents, who then in turn teach the interns and medical students as they rotate through the various clinical services." Results of formal teaching exercises such as having blood center personnel speak at grand rounds, staff meetings, or in-service training programs, have been varied (262). As discussed with respect to fresh-frozen plasma and albumin, textbooks in general use by physicians do not always follow the guidelines promulgated by blood bankers.

The rise of component therapy has exacerbated the need for clinicians to become more sophisticated about the use of blood. As a consequence, several books of guidelines directed at practicing physicians have been published. A pocket-sized book published by AABB seems the most accessible (i.e., in addition to being pocket-sized, it has brief chapters, is indexed, and costs only \$3). An AMA guide, *General Principles of Blood Transfusion* (39), has gone through several editions (1970, 1973, 1977) and is being revised. Currently, the AABB is engaged in a more active attempt at physician education. Its *Physician's Handbook* is to serve as the basis for a new physician self-assessment program, the *Transfusion Medicine Self-Assessment Program* (26). Other attempts at continuing medical education include the American College of Surgeons' recent postgraduate course, *Pre- and Postoperative Care: Blood and How to Use It* (36).

Perhaps the most encouraging trend in physician education is the institution by the National Institutes of Health of "Transfusion Medicine Academic Awards" (403; see app. A), and other efforts concerning appropriate use. Recipients of Transfusion Medicine Academic Awards will work with local medical schools to incorporate

transfusion medicine into the curriculum. Currently, five such awards, at \$50,000 per annum for 5-year periods, have been granted. The program will be announced each year until needs in transfusion medicine are fulfilled. Perhaps as important as the awards themselves is the fact that current transfusion medicine award recipients are communicating with each other about their experiences in inculcating local changes (534). In addition, applicants for National Research and Demonstration Center in Transfusion Medicine (NRDC) awards are encouraged to design projects directed at testing and evaluation of strategies to affect health management practices and physician and health-professional knowledge.

As encouraging as these attempts at more physician education are, a limiting problem is that many indications for transfusion are based on "soft" scientific data. Thus, guidelines conflict and experts conclude by saying that it is impossible to provide rules of thumb. There is a need for more objective evidence, but few randomized clinical trials have been conducted. For example, even though NIH has stressed the need for clinical trials and applicants for NRDC and Specialized Centers of Research in Transfusion Medicine (SCOR) awards are encouraged to conduct controlled, carefully monitored trials, support for such trials **alone** is explicitly prohibited by the awards. Currently, however, clinical trials are under way on the appropriate uses of platelets (at Puget Sound), Factors VIII and IX (at the San Francisco Veterans Administration Medical Center), and fibronectin (Albany, NY) (532).

### Blood Center and Hospital Controls

Attempts to educate physicians and blood bank personnel as to the appropriate uses of blood products, while useful, typically have had limited impact. Accordingly, some blood centers and hospitals have made more direct attempts to modify the use of blood products. At Puget Sound Blood Center, for example, requests for more than eight units of a blood component must be cleared through a blood center consultant before the blood is released. This consultation process is an example of the extent to which blood center physicians have gone from laboratory to clinical aspects of transfusion (532).