Introduction and Summary

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Introduction and Summary

INTRODUCTION

A decade ago, national interest in assuring an adequate and safe blood supply resulted in a pronouncement by the Federal Government of a National Blood Policy (NBP), with the four general goals of improving supply, quality, accessibility, and efficiency. Among the policies that were to be implemented were the adoption of an all-voluntary blood collection system, resource sharing and regionalization of blood collection and distribution, and programs to assure appropriate use.

In addition, information systems were to be developed on a continuing basis to monitor: 1) the whole blood collection system for transmissible diseases and transfusion mishaps to aid in improving the effectiveness of the blood banking system; and 2) the source plasma and plasma fractionation sector to determine the sufficiency of domestic sources of plasma fractions, develop future positions on the relationships between plasmapheresis and plasma fractionation and whole blood banking, and determine the degree of interdependence between the United States and other countries with respect to plasma and plasma products. Adherence to the highest attainable standards for blood products were to be achieved through Federal regulatory authority, and research on all aspects of blood products was to be supported.

Despite a flurry of legislative activity preceding the announcement of the National Blood Policy, no legislation was actually enacted. The announcement of the NBP by the Secretary of the Department of Health, Education, and Welfare (DHEW, the precursor to the present Department of Health and Human Services, DHHS) became the focal point around which blood banking policy has evolved over the past decade.

Following announcement of the National Blood Policy, the Federal Government accepted, and partially funded, a private sector plan to establish an American Blood Commission (ABC) to implement "the lion's share" of the NBP. A number of factors have inhibited the ABC's effectiveness in implementing the NBP: the Commission had no enforcement power; its long-range financial support was dependent on the blood resource organizations which were already involved in the functions that ABC was expected to influence; and many of the factors that contribute to improvements in blood resources (e.g., development of new technologies) were outside ABC's reach. However, ABC succeeded in providing a forum in which blood banking issues could be openly discussed, and much of the conflict among blood bankers of a decade ago is gone today.

ABC, because it was initiated in response to the call for a National Blood Policy, has been the NBP's most visible activity. Because the National Blood Policy represented a pluralistic, private sector approach instead of a central, Government-directed approach, its primary contribution over the past decade has been its acceptance as a general guiding principle by both the private and public sectors, infusing a sense of common purpose into all contributors to our blood resources. The Policy may have been sufficiently general in purpose so that few interest groups felt seriously threatened by it. Whatever its real or imagined impact, however, many of the problems areas identified over a decade ago have shown substantial improvement.

Of course, other problems remain or have arisen since the NBP was announced, and, for the first time, technologies are being developed that could replace many, if not eventually all, of the products currently obtainable only from human blood. Some of these new products, especially the major derivatives (albumin and antihemophilic factor) currently extracted from plasma, may be commercially available before the end of the 1980s.

This study was conducted at the request of the House Committee on Energy and Commerce. The committee pointed out that questions remain concerning donor screening and selection, the appropriate Federal reaction to the changing pattern of blood-related transmissible diseases, the efficiency and coordination of blood banking systems, emerging and future technologies for blood-function substitution, and whether there is a constructive role for a National Blood Policy.

Progress in blood resources over the past decade, and current and future technologies, are the subjects of this report. The rest of this chapter summarizes the major issues in blood banking policy and focuses on specific points within each issue area that deserve continuing attention.

Chapter 2 presents a brief overview of Federal interest in maintaining and improving the Nation's blood resources, the blood products used in therapeutic applications, the donors who provide blood, and Federal activities in blood resources.

Chapter 3 describes the blood services complex: the voluntary, whole blood and blood components sector; and the commercial plasma and plasma derivatives sector.

Chapter 4 describes the blood technologies: technologies for blood collection and processing; and plasma fractionation technologies.

Chapter 5 discusses current issues: the impact of AIDS on blood collection and use; coordination of blood resources; the impact of health care cost containment efforts on blood resources; and issues of appropriate use of blood products.

Chapter 6 provides a look at alternative technologies: alternative sources and substitutes for blood products. ‘

Chapter 7 considers future directions for blood banking: voluntary v. commercial approaches; and tissue and organ banking and blood centers' interests in these activities.

SUMMARY

The Blood Services Complex

The structure of the blood resources system remains nearly the same as it was 10 years ago, but it is very different in terms of the products, services, and technologies offered. The system continues to consist of two essentially different sectors: 1) a largely voluntary whole blood and components sector, and 2) a largely commercial source plasma and plasma derivatives sector. (Products separated from whole blood [red cells, platelets, cryoprecipitate, and fresh-frozen, single-donor plasma] are usually referred to as "components," while products derived from plasma [albumin, Factors VIII and IX, the immune globulins] are called "derivatives.")

Three types of facilities are involved in the voluntary sector: 1) community and regional blood centers which collect and distribute blood to hospitals in circumscribed geographic areas, 2) hospital blood banks which both collect and transfuse whole blood and components, and 3) hospitals which primarily store and transfuse blood but do not collect it. These facilities are represented by several organizations with overlapping memberships.

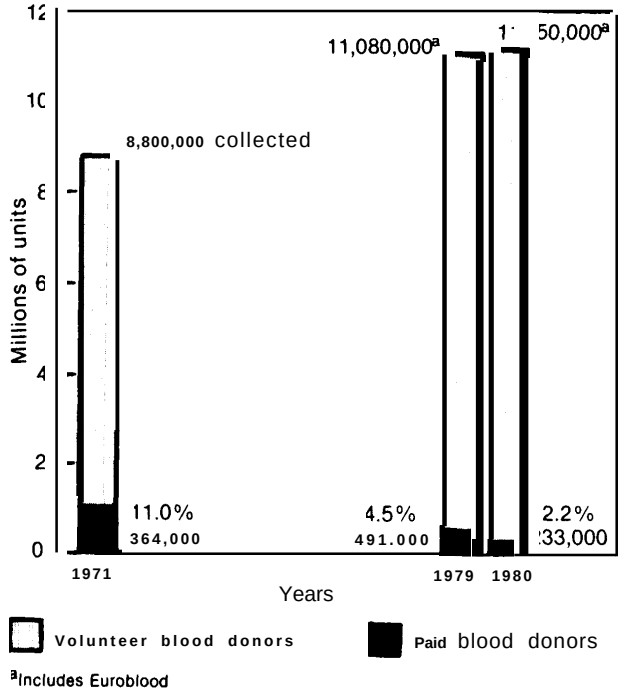
The American Red Cross (ARC) has 57 regional centers operating under a single Federal license. These Red Cross regional centers cover about half the geographic area of the United States and collect about half of the Nation's whole blood. The institutional members of the American Association of Blood Banks (AABB), including members who belong to the Council of Community Blood Centers (CCBC), collect another 45 percent of the Nation's blood. In 1980, seven ARC regional centers and all but two CCBC centers also belonged to the AABB, as did 1,977 blood collecting hospitals. One hundred and one community blood centers were members only of AABB and did not belong to CCBC. Approximately 2 percent of blood was collected through 16 unaffiliated blood centers.

The trend has been for hospital blood banks to play less of a role in blood collections. In 1971, 69 percent of the blood collected came from regional and community blood centers (555). By 198o these centers collected 88 percent of the total, increasing to 91 percent in 1981 (29). The increasing predominance of regional and community centers has been attributed to their ability to collect blood through constant mobile collections. In 1980, nearly 70 percent of whole blood collections was through mobile units.

Whole blood collections have been able to keep up with increasing demand while paid whole blood donations have decreased significantly (fig. 1). The ability to meet increased demand has occurred through increased recruitment, improved inventory management, technologies that have increased the storage life of blood and its components, and a large increase in the use of blood components instead of whole blood. Between 1971 and 1980, whole blood collections increased from 8.8 million to 11.15 million units per year, while whole blood and red cell losses decreased from 2.44 million to 1.15 million units, an improvement in losses from 28 to 10 percent of blood collected. Out of the 11.15 million units collected in 1980 (fig. 1), 14.8 million units of blood components were transfused, exclusive of blood that was outdated or lost (fig. 2).

The source plasma sector, on the other hand, is largely commercial and has two main components: 1) collectors, or plasmapheresis centers; and 2) fractionators. Not-for-profit blood banks and blood centers also play a part in the commercial plasma industry when they sell recovered or salvaged plasma (plasma recovered after components have been removed from whole blood, or salvaged after whole blood has outdated) to fractionators; when they contract with commercial firms to fractionate their plasma into derivatives which they then market themselves; or, in one case, when they fractionate and market their own products. Approximately 45 percent of the Red Cross' recovered plasma is fractionated by commercial fractionation companies, and 17 to 20 percent of the plasma derivatives sold in the United

Figure 1 .-Collection of Whole Blood in 1971, 1979, and 1980



[a]Includes Euroblood

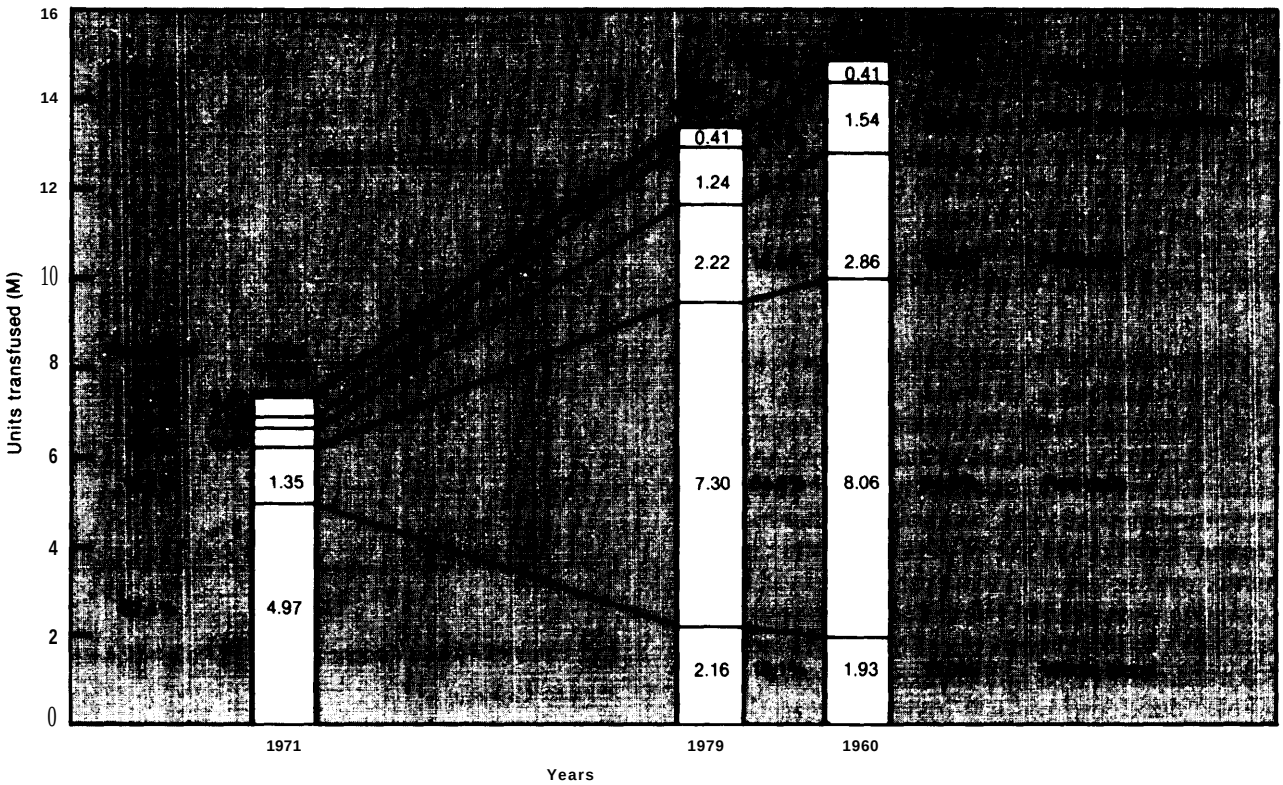
SOURCE: Surgenor and Schnitzer/ABC, 1983.

States is sold by the voluntary sector (primarily the Red Cross and the New York Blood Center).

There are 336 source plasma centers licensed by the Food and Drug Administration (FDA), 317 of which are commerciall, operated, and 19 of which are operated by community or Red Cross blood centers. More than 90 percent of the source plasma centers are owned by **30** companies which market biological products. Some of these biological companies are in turn subsidiaries of larger corporations (e. g., Sera-Tec Biological, owned by the Rite-Aid Corp., operates nine centers in the East and Midwest, most of which are located near college campuses).

Plasma collected by commercial plasmapheresis centers is either sold to U.S. fractionators who separate it into a number of products (primaril, albumin, Factor VIII [antihemophilic factor] and immune globulins), ***or*** exported to fractionators in Europe, Japan, or South America. The way plasma is provided from plasmapheresis centers to fractionators varies. Four fractionation com-

Figure+ 2.–U.S. Transfusions of Blood and Components, 1971-80



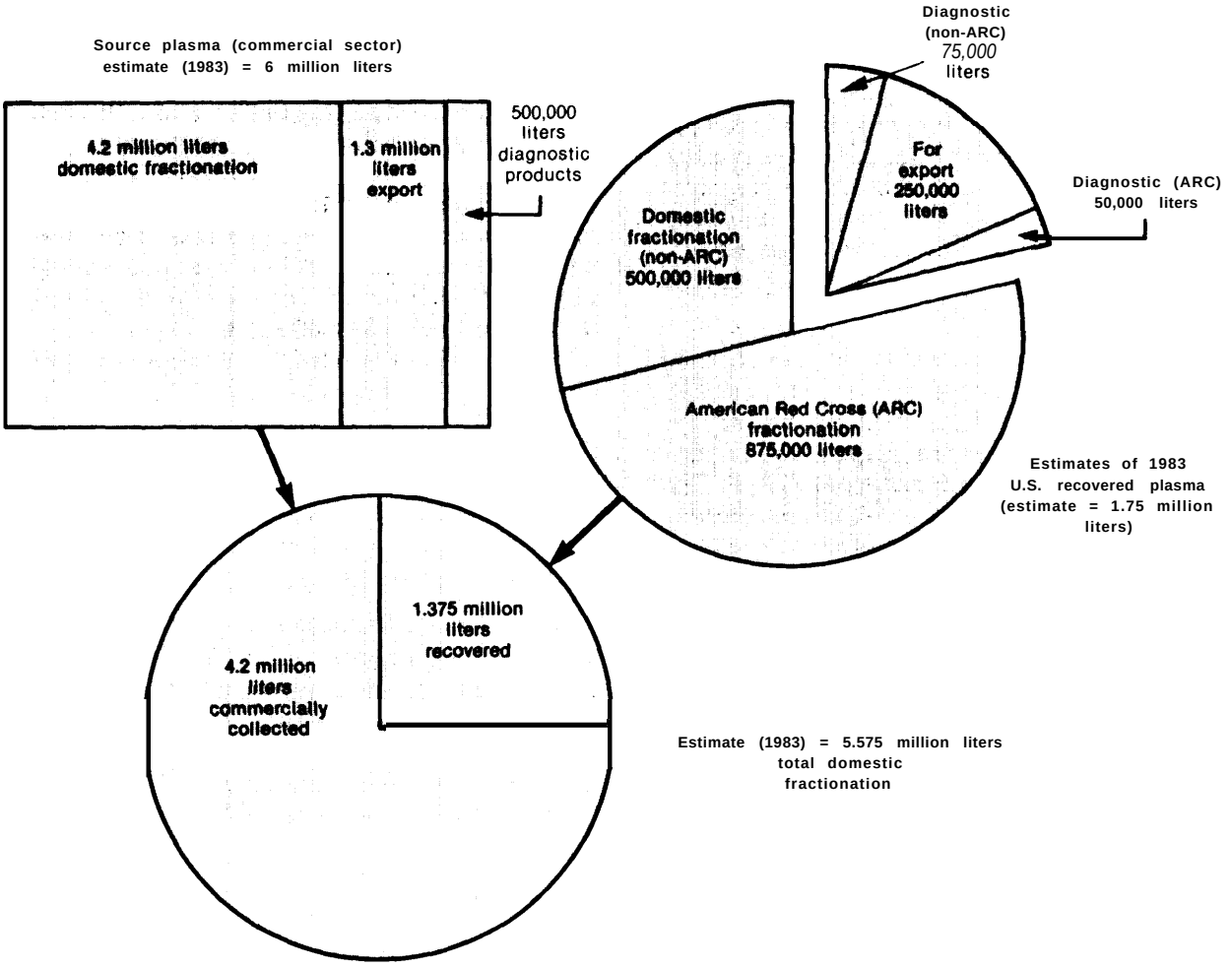
SOURCE: Surgenor and SchnitzerlABC, 19S3.

panics "self-source"; i.e., they run their own source plasma centers. Ninety-eight U.S. source plasma centers (30 percent) are owned by fractionation companies. In addition, most of the other centers contract annually with fractionators to provide a certain amount of plasma, although there is some "spot buying." Recovered plasma (from whole blood) is either contracted for, or marketed through the efforts of nine major brokers. Both the brokers and the for-profit source plasma centers are members of the American Blood Resources Association (ABRA), a nonprofit trade association organized in 1972 to represent the interests of businesses engaged in the collection, manufacturing, or distribution of certain biological products—in particular, plasma for further manufacturing.

The market for source plasma is largely controlled by four pharmaceutical companies (Hyland Therapeutics, Cutter Laboratories, Alpha Therapeutics, and Armour), which are in turn subsidiaries of major corporations (Travenol, Bayer, Green Cross of Japan, and Revlon, respectively). Each commercial fractionator accounts for about 1 million of the 4 million liters fractionated commercially in the United States annually (459). In addition, the nonprofit New York Blood Center operates its own plant, with a capacity to fractionate 300,000 liters per year from plasma recovered from its own donors and from a portion of Red Cross donors.

The U.S. source plasma collection industry is the most important contributor to worldwide plasma fractionation. The approximate disposition of both source and recovered plasma collected in the United States at the present time is shown in figure 3. About 1.3 million of the 6 million liters of source plasma produced is exported, in addition to the export of plasma derivatives manufactured in the United States. Some 5.5 million of the 12.5-million-liter worldwide manufacturing capacity in 1978 was in the United States.

Figure 3.—Disposition of Domestically Collected Plasma, 1983



SOURCE: Understanding Plasma, *Plasma Quarterly*, 1984.

Of the 7. O-million-liter capacity outside the United States, abouts million liters were in the commercial sector, and about 2.0 million liters in the voluntary sector. But there were only about 77 plasma fractionation firms worldwide outside the United States (439) and commercial plants outside the United States operate at about 60 percent capacity, compared to about 85 to 90 percent in the United States (459). Increasing amounts of the albumin and antihemophilic factor (Factor VIII) produced in the United States are used abroad. In 1984, it is estimated that approximately one-third of the albumin and one-half of the Factor VIII produced in the United States will be consumed in foreign countries (see table 19). The U.S. fractionation industry currently supplies about 70 percent of Factor VIII, 70 percent of albumin, and lesser amounts of the gamma globulin used in the world. Thus, much of the plasma and plasma derivatives used worldwide comes from U.S. sources.

Costs of Blood Products

Blood collection and transfusion facilities have not developed an industrywide uniform method of allocating costs to each step in the collection and transfusion process. Further, most of the available data are on charges or prices, not on costs.

In 1980, the average cost to a community blood center for the collection of one unit of whole blood was nearly $46, but costs varied widely, with a standard deviation of over $15. Most of these costs are allocated to red cells (see, e.g., 142). In 1980, the average community blood center red cell processing fee was about $32, while the average total hospital charge for a unit of red cells was about $89. Processing fees charged for whole blood and packed red cells are less than the cost per unit of blood collected because costs are also allocated to other components.

There are wide variations in the fees charged to hospitals by blood collectors and by hospitals to patients. For example, in 1983, processing fees for whole blood charged to hospitals by American Red Cross regions ranged from $28 (in San Juan, PR) to $59 (in San Jose, CA). Some of these differences can be explained by differences in costs between geographic areas, but blood centers can allocate more costs to one component than to others (as in the case of red cells), and also factor into their charges such program expenses as personnel training, research support, and capital costs for new buildings and equipment. There are also substantial variations in hospital charges for red cells (the only component for which hospital data are available), with standard deviations from a quarter to a third of the mean (576).

In addition to the processing fee charged by the blood center, hospital charges might include an additional processing fee, a nonreplacement charge if a replacement policy is still in effect, a laboratory charge, an infusion charge, and other charges. Total charges are usually higher at collecting than at noncollecting hospitals, with higher processing fees and nonreplacement fees accounting for the higher total charges (576). (Latest available data on hospital charges are for 1980, and such charges have undoubtedly risen since then.)

Increases in blood costs have generally not exceeded increases in total health care costs. From 1980 to 1982, national health expenditures increased an average of 15 percent per year, while blood center processing fees increased 7 percent (for CCBC members) and 12 percent (for Red Cross regions). Increases in hospital charges for blood, on the other hand, appear closer to increases in hospital charges in general, although it is difficult to draw conclusions with information from only 2 years.

As for costs of plasma derivatives, 1984 retail prices for Factor VIII (including heat-treated products) ranged from $0.09 to $0.26 per unit in the United States (99,464). Needs vary for mild, moderate, and severe hemophiliacs, but assuming an average consumption of 50,000 units per year (293), Factor VIII could cost the average hemophiliac from $4,5OO to $13,000 per year. In addition, from 10 (99) to 15 (76) percent of hemophiliacs have inhibitors to Factor VIII and require a special form of coagulation product, anti-inhibitor coagulant complex, which can cost from $0.70 to $1.00 per unit (99). Factor IX Complex, used for hemophilia B patients, costs from $0.05 to $0.10 per unit. Products for hemophiliacs are more costly in foreign countries.

In the United States, a 250-milliliter bottle of albumin costs approximately $32. The price of albumin has not been challenged per se, but its use instead of less expensive crystalloid alternatives for volume restoration has been questioned, and there have been other longstanding questions over the proper use of albumin.

Availability

The trend in collection and distribution of blood components has been toward centralization; i.e., toward the establishment of community and regional blood centers and away from hospital blood banks individually providing for their own needs. Blood components, especially the cellular ones, still have relatively short storage lives; whole blood and red cells have 35 days (with preservative solutions recently approved for 49 days), and platelets up to 5 days (5-day storage bags have recently been approved, increased from 3-day bags). Thus, the regionalization of blood resources has been primarily oriented toward maximum use of a perishable product, and purchasers (predominantly hospitals) have been less concerned over the price they paid than the assurance that they could obtain blood components as needed. That is, the cost to hospitals could be passed on to pa-

tients and their insurers; so availability, and not price, was the primary factor in purchasing blood components. (The implications of present health care cost containment measures and their effect on price-consciousness are discussed below.) Regionalization of blood resources has proceeded on this basis, including the American Blood Commission's regionalization recognition program.

Blood banks, whether as regional centers or as part of a hospital, have also kept their stocks in approximate balance with demand by sharing between banks with surpluses and those with shortages. There is apparently much undocumented ad hoc sharing by blood banks both within regions and between regions, and there are also two national sharing programs, one run by the American Association of Blood Banks, and another by the American Red Cross.

Periodic attempts to combine these two systems into a single system, with the American Blood Commission as the mediator, have been unsuccessful. One reason is that, despite a Department of Justice opinion that a resource sharing agreement would not violate Federal anti-trust legislation, the American Red Cross has expressed fear that it would be liable to a civil suit if it were to sign a formal nationwide resource sharing agreement. For example, representatives of the plasma derivatives industry have objected to limiting a resource sharing agreement to voluntarily collected blood. On the other hand, there are no systematic deficiencies which can be clearly identified which would be resolved by a single sharing system. Blood banks have their own informal networks and ***use*** both of the national systems on an as-needed basis. In addition, sharing can and does take place on a regular, planned basis between blood banks with chronic shortages and those which have a consistent surplus.

It is not possible to estimate what the minimal amount of sharing should be between blood service regions to determine whether regions are collecting their "fair share" of the blood components they need and use; i.e., whether they are adequately self-sufficient. Blood collection regions have been established reflecting past blood collection organization efforts, the distribution of hospitals in the region, as a compromise between competing local collectors, etc. They have not been established on the basis of assuring that the population base from which blood is collected is the same population as the users of those blood products. Nor would that be possible, given the widespread population that modern medical centers draw from. Similarly the majority of donors are under 40, while the majority of users are older people, and blood collected from small cities and towns is used in large cities.

In conclusion, there do not seem to be systematic problems with availability in the voluntary whole blood sector. Imbalances between supply and demand have been met both within and between regions by a combination of ad hoc and organized methods of sharing. Price has not played much of a role, but indications are that it is becoming increasingly important as purchasers come under prospective payment systems and can no longer pass on all the costs of their purchases.

Because the plasma derivatives sector is part of the pharmaceutical industry its distribution networks are similar to those for the marketing of prescription drugs. Thus, the commercial sector presents a different picture from that of blood components, although, as in the voluntary sector, availability of products does not seem to be a problem. The national plasma derivatives market is intertwined with the international market, and both profit and nonprofit companies and organizations are involved. Because of the increased use of red cell concentrates instead of whole blood, the voluntary sector has become a significant supplier of plasma and plasma derivatives, accounting for about 20 percent of the plasma derivatives sold in the United States. The American Red Cross (which contracts with commercial fractionators to produce derivatives from Red Cross plasma) markets its own products, as do the New York Blood Center, and laboratories run by the States of Michigan and Massachusetts. In addition, both the Swiss and Dutch Red Cross sell some albumin in the U.S. market. The New York Blood Center and the American Red Cross also sell Factor VIII, and the Massachusetts Biologics Laboratory is the sole producer in the United States of herpes zoster immune globulin.

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Following the establishment of the plasma fractionation industry in World War II to produce albumin in mass volume, albumin for civilian use became the principal product of the industry. This "driving force" role was briefly taken over by the immune globulins in the 1950s, then by the coagulation proteins (principally Factor VIII) toward the end of the 1960s as techniques to extract coagulation proteins in mass volumes were perfected. At the present time, coagulation proteins, being the most profitable, are the principal desired product of the fractionation industry, and albumin is a "byproduct" although still the largest in terms of volume and total sales (see table 1). Hyperimmune globulins against specific diseases have been developed in addition to general immune serum globulins that contain a mixture of antibody types.

Albumin marketing is much like that for basic commodities or generic drugs. The market is sensitive to price changes, a high level of competition exists, and product choice is related more to the price, source of service, packaging, and other inducements than to the quality of a particular manufacturer's product. All manufacturers' products must meet FDA standards.

Distribution outlets for the coagulation proteins vary from region to region, but most large urban areas have at least one major hemophilia treatment center that routinely stocks them. As home care of hemophiliacs increases, patients are beginning to be able to have these products supplied directly to them on prescription. Packaging, auxiliary supplies (e.g., infusion sets), availability, as well as price and brand name loyalty have begun to determine which manufacturer's products are purchased. In addition, some manufacturers provide financial assistance in the form of reduced prices for insured hemophiliacs. Product availability may be an issue, however, for those who are uninsured or live in remote areas.

Sellers of both albumin and the coagulation proteins have central distribution or supply networks, and volume purchasing, often by organized groups of purchasers, on an annual bidding basis, is fairly prevalent. Immune globulins are routinely distributed by pharmaceutical distributors, hospital supply companies and blood centers, as well as directly by manufacturers to the numerous hospitals, nursing homes, physicians, and clinics that prescribe these preparations. Annual bidding is not as common as for albumin and the coagulation proteins, but is increasing.

In sum, regional shortages and surpluses in the voluntary sector have been handled through sharing programs between regions, but there is much ad hoc sharing between blood banks outside the organized intra- and interregional programs. Technological improvements in storage methods have also enhanced availability. Price and other competitive aspects of supplying a product have not been important factors but may become so with the implementation of programs to contain health care costs through prospective payment systems.

In contrast, the major plasma derivatives are marketed nationally and internationally, with no apparent advantages in price and quality of the nonprofit products over the commercial ones. Excess plasma from greater use of red cell concentrates instead of whole blood has led to nonprofits becoming increasingly involved in the plasma derivatives industry. Product availability seems to be an issue only for hemophiliacs, as a consequence of inadequate resources or geographic inaccessibility to treatment.

Table I.—Worldwide Demand for Plasma Fractions, by Product, 1978 (in monetary value)

Albumin/PPF	41 %
Intravenous gamma globulin	23
Hyperimmune globulins	14
Factor Vlll concentrate	13
Immune serum globulin	8
All others	1
Total	100°/0

SOURCE: **International Federation of Pharmaceutical Manufacturers, 1980,**

Safety

Although recent attention on the safety hazards of blood transfusions has focused on acquired immunodeficiency syndrome (AIDS), individuals have a much greater chance of contracting some form of hepatitis from transfusions of blood components and some plasma derivatives than they do of contracting AIDS, despite a number of med-

ical advances and the decrease in paid whole blood donors. Laboratory tests for hepatitis B have greatly increased in sensitivity over the past decade; as a consequence, there has been a dramatic reduction in posttransfusion hepatitis B cases. (Hepatitis A is rarely transmitted by blood because the individual's blood usually contains the virus only during the clinical stage, during which the individual is unlikely to donate blood and which is easily detected during routine donor screening procedures.) However, by the late 1970s, a new type of transfusion-associated hepatitis was found.

This form of hepatitis has been named non-A, non-B hepatitis, because it is distinctly different from both hepatitis A and B. Five to eighteen percent of Americans who receive five or more units of transfused blood develop non-A, non-B hepatitis (271a). Currently, approximately 90 percent of all posttransfusion cases of hepatitis is due to non-A, non-B hepatitis, and 10 percent due to hepatitis B (558). No etiologic agent(s) has so far been identified, although a retrovirus has recently been implicated as the cause of non-A, non-B hepatitis. Therefore, there are no specific tests for non-A, non-B hepatitis at present.

Efforts to prevent infection can occur at the following stages of blood processing: 1) donor screening, to prevent collection of potentially contaminated units; 2) laboratory testing of collected units, to detect contaminated units; and 3) inactivation or removal of micro-organisms, to destroy infectious agents prior to use.

Screening of donors may begin by selection of populations with a low prevalence of transmissible diseases. Preference for voluntary over paid donors was based, in addition to ethical considerations, on the lower prevalence of hepatitis and other transmissible diseases in voluntary donors. The exclusion of intravenous drug abusers is based on the same considerations, and recent decisions to ask homosexual and bisexual men with multiple partners to refrain from donating, due to the high incidence of AIDS in this group, were similarly motivated.

Individual donor screening is also carried out. Each prospective blood or plasma donor, whether voluntary or paid, is subjected to screening by medical history and selected physical and laboratory examinations. Prospective donors are questioned for signs and symptoms of disease and a history of exposure to disease. Laboratory tests to determine whether or not the collected unit may transmit infection may be specific or nonspecific. Specific tests, such as the test for hepatitis B surface antigen, which is required of all blood and plasma donors, detect the infectious agent itself or some element of it. Nonspecific tests, such as the screening for syphilis that is also required of all blood and plasma collections, usually measure a response of the body which may occur in several disease states, one of which includes the disease in question. They have obvious limitations but may be useful until specific tests can be developed. Other examples of nonspecific tests are measurement of the liver enzyme, alanine aminotransferase (ALT), used by a few blood centers to screen for carriers of non-A, non-B hepatitis, and the T-lymphocyte helper: suppressor ratio, which was initiated at the Stanford Medical Center to screen for AIDS. The presence of antibodies to hepatitis B core antigen (as contrasted to the presence of hepatitis B surface antigen, which is indicative of the presence of the active virus) has been used by some blood centers to screen donors for AIDS, because it is believed that those individuals who have been exposed to hepatitis B may also have a higher risk for exposure to AIDS.

To be useful, laboratory tests should be: 1) able to be performed easily, rapidly, and on a large scale to permit testing of the large number of units collected to prepare perishable blood products; 2) sensitive enough to detect a large proportion of contaminated units; 3) specific enough not to have incorrectly positive reactions in most noninfected units; 4) able to detect a disease of health importance to the recipient population; and 5) targeted at a disease which occurs frequently enough to warrant screening of all donated units (434). Of the tests mentioned above, the specific test for hepatitis B surface antigen is the only test that satisfies all these criteria.

Early attempts to prevent AIDS from entering the blood supply were reminiscent of early methods oriented toward hepatitis B and current attempts to screen out hepatitis non-A, non-B carriers. One of the principal stimuli for a National Blood Policy was the risk of hepatitis B. Donor screening methods, directed both at groups with high incidence of hepatitis and at individuals, plus the labeling of blood as being derived from "paid" or "voluntary" donors, were the principal methods of screening for hepatitis B until very sensitive laboratory tests to detect the presence of the hepatitis B surface antigen were developed and applied to every unit of blood and plasma collected. In the case of non-A, non-B hepatitis, donor screening remains the primary line of defense, with a few blood centers using the nonspecific ALT test in addition. This is similar to strategies to screen for AIDS; specific classes of donors have been excluded, physical examinations in high risk areas look for some of the preclinical signs of AIDS such as general enlargement of the lymph nodes, and a few blood centers have used surrogate tests for AIDS. (A specific blood test for the presumed AIDS agent, human T-cell lymphotropic virus, type III (HTLV-III), will be available in early 1985.)

In addition to screening through donor exclusion and laboratory testing, some transmissible infections can be prevented by treatment of the blood product to remove or inactivate infectious agents. Currently, the most important of these methods is pasteurization. (The cellular elements of blood cannot withstand this treatment, which is applicable only to some of the plasma derivatives.) Albumin, which is widely used for blood volume expansion and other medical purposes, can be heated to 600 C for 10 hours, which inactivates hepatitis viruses and appears to inactivate other viruses as well. Thus, FDA requires that all albumin preparations be pasteurized in this manner.

Prior to the AIDS problem, concentrates of the clotting factors (e.g., Factor VIII) had not been subject to pasteurization because of inactivation of the clotting factors. However, recent advances in heat processing of Factor VIII in the presence of stabilizers have been accomplished, with evidence of inactivation of some type of viruses but with some loss in potency of the preparations (162). All four commercial manufacturers of Factor VIII have recently received FDA approval to market these products. Claims of reduced hepatitis transmission from heat-treated products, based on chimpanzee studies, are currently under study, with the hope that pasteurization will also inactivate other viral agents, such as the presumed virus(es) for AIDS. (Current research suggests that the presumed AIDS agent, HTLV-III, is inactivated by this process.)

ISSUES AND POINTS TO CONSIDER

Currently, three areas of primary concern in blood resources development and maintenance are at issue, none of which were major issues a decade ago when a National Blood Policy was enunciated. These issues are: 1) the impact of AIDS on blood collection and use, 2) the impact of efforts to contain health care costs and the related issue of the costs of blood products, and 3) alternative sources and substitutes for blood products. AIDS is having an immediate impact, health care cost containment portends possible fundamental changes in the near future, and new and emerging technologies have the potential in the not too distant future to profoundly affect the present source plasma and plasma fractionation and voluntary whole blood industries.

In contrast, the primary issues a decade ago, in addition to that of safety, were: 1) coordination of blood resources (including disagreement over community v. individual responsibility for blood donations, and the desirability of Federal intervention in the blood supply); 2) appropriate use; 3) voluntary v. commercial approaches; and 4) information systems to monitor blood resources. These are still issues today, although they

been pushed into the background by AIDS, costuse of clotting factors as the suspected mode of containment, and alternative sources. Furthermore, continuing activities in these areas are likely to be influenced by what happens in the three current primary issue areas.

AIDS

In some sense, the safety issues associated with AIDS and blood products are but an extension of the safety issues of a decade ago, when hepatitis B was the primary disease that was transmitted through blood. Hepatitis continues to be the primary blood-transmitted disease, with non-A, non-B hepatitis replacing hepatitis B as the primary transmitted disease. The experience with non-A, non-B hepatitis is very similar to that with AIDS, with the difference that it has not captured the public's attention as AIDS has. Of the risks associated with blood products, transfusion recipients and users of coagulation proteins are much more likely to contract non-A, non-B hepatitis or hepatitis B than AIDS. Hemophiliacs, however, are a special class even though their rates of hepatitis are higher than their risk of contracting AIDS, because of their great use of coagulation proteins and the high incidence of AIDS among them.

Publication in January 1984 by Centers for Disease Control (CDC) researchers of their conclusion that there were cases of AIDS associated with transfusions (143) caused consternation in blood resources circles. But at a February 1984 meeting, convened by CDC, of representatives of blood banks and other groups interested in transfusion-associated AIDS, there was agreement that the evidence that AIDS could and had been transmitted through blood products was conclusive enough that no further studies need be conducted to prove/disprove the association. Rather, studies to quantify and clarify the risks were needed. Even before this, however, AIDS was already suspected as being due to some type of transmissible agent such as a virus, and procedures had been adopted in an attempt to reduce the risk of blood-related AIDS. Furthermore, it was already known in 1982 that hemophiliacs were among the groups that were at increased risk for AIDS, with their heavy transmission.

In March 1983, the 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 (NIH), issued recommendations to initiate: 1) educational programs to inform persons at increased risk of AIDS to refrain from blood or plasma donation, 2) expanded medical screening of blood and plasma donors to identify individuals with early signs or symptoms of AIDS, 3) examination of source plasma donors for lymph node enlargement, and 4) measurement of body weight of source plasma donors prior to each donation to detect unexplained weight loss. Some blood banks began to introduce 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.

As part of public information campaigns about the risks of AIDS, the Public Health Service and blood banking organizations included warnings about who should refrain from donating blood and also tried to allay groundless fears that AIDS could be contracted by simply donating blood. For source plasma collectors, FDA made additional recommendations that plasma collected in geographic areas of high risk for AIDS not be used to manufacture coagulation proteins. And the National Hemophilia Foundation issued guidelines for the use of cryoprecipitate, Factor VIII and Factor IX complex, including the preferential use of cryoprecipitate in some circumstances.

As of May 1984, the FDA Blood Products Advisory Committee was also studying the issue of whether specific surrogate tests should be instituted for all whole blood and plasma collections and had 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 (as had been

adopted by a number of blood banks for whole blood donations).

All four commercial manufacturers, the Red Cross, and the New York Blood Center withdrew lots of Factor VIII (and related lots of Factor IX Complex) upon being informed that a donor(s) whose plasma had been used in the preparation of those lots had developed AIDS. (Donor records must be kept for at least 5 years, and matchups of AIDS cases with donor lists had been made.) The largest of these voluntary market withdrawals involved enough Factor VIII to represent 500 patient-years of treatment (434).

As noted, all four commercial manufacturers also subsequently developed heat-treatment (pasteurization) methods with claims of reduced infectivity of hepatitis viruses, the hope being that the process would also affect the presumed AIDS virus. These pasteurization methods have reduced the potency of the clotting factor preparations (the reason why previous preparations could not be pasteurized), but apparently not enough to markedly affect their efficacy.

Surrogate laboratory tests for AIDS have also been extensively discussed, and some blood banks have instituted them. The tests 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. However, conditions other than AIDS can lead to abnormal test results in tests of the first type. For example, Stanford University Blood Bank began to test all blood donations for T-lymphocyte helper: suppressor ratios (445). About 1 to 2 percent of collections have been positive, but such individuals are not permanently deferred from donating, since short-term virus infections can also cause an abnormal ratio.

The Irwin Memorial Blood Bank in San Francisco instituted a test for antibodies to hepatitis B core antigen (as did Cutter Laboratories for its source plasma donors) which reveals past infection with hepatitis B and expects that donor deferrals will increase by 5 to 7 percent. (Cutter expected a positive test rate of 15 percent and planned to use this plasma only for production of albumin and immune globulins, which are not implicated with AIDS.)

AIDS also kindled interest among patients and physicians for autologous and directed donations. Autologous donations, where a patient "banks" his/her own blood prior to elective surgery, was always considered the safest of transfusions. However, it could pose problems for the management of blood if it were to be more widely applied. Surgeons often prefer not to use it, medical personnel may be exposed to health risks because the blood is not tested for hepatitis, and autologous blood may outdate if surgery is postponed. Individual blood banks have allowed the use of directed donations either to ease patients' fears or in response to pressures from patients and their physicians. Directed donations, however, have been opposed by most blood bankers because of the potential for disruption of the blood collection and distribution system if widely adopted, and because of a lack of evidence that such donations are indeed safer than anonymous donations.

In April 1984, the Secretary of DHHS announced that researchers had identified the AIDS virus and developed technologies to mass-produce a blood test which would become "widely available within about 6 months, " and would "identify AIDS victims with essentially 100 percent certainty" (256). A few days later, DHHS announced a request for applications to produce and distribute such a test, with requests to be submitted within 10 days of the announcement (181). Thus, whether the Secretary's promise to provide a reliable test for AIDS can be kept will be known soon, and if the test is provided it should alleviate much of the pressure to adopt some type of surrogate test—and may again turn directed donations into a nonissue in the blood community.

But questions raised as a result of the donor screening methods developed against AIDS, use of surrogate tests, and interest in directed donation programs will not be completely moot even if a highly specific test for AIDS is available soon.

Points to Consider

Evaluation of Donor Screening Criteria .-One of ***the first steps taken by the blood community in attempting to keep AIDS out*** of ***the blood***

supply was to exclude classes of people who were deemed at high risk for AIDS. The impact of this policy has been especially felt by the gay male community. (Young males have always been among the principal, if not the largest, groups of blood donors.) Intravenous drug abusers have always been one of the excluded blood donor groups, and exclusion of recent Haitian immigrants can be likened to policies which exclude donors who have recently arrived from areas with high incidence of infectious diseases which can be transmitted through blood donations.

An evaluation of the exclusion of gay males is needed, not only to confirm whether or not this policy has indeed led to decreased AIDS transmission through blood, but also to confirm whether or not such an exclusionary, stigmatizing policy is justified by the results.

There are two measures of whether or not this policy has worked. First is an assessment of the process; i.e., whether or not the donor population has indeed changed, with fewer young to middle-aged males in the donor base. This would be especially significant in areas of high incidence of AIDS, where the implementation of this policy has been actively pursued. This evaluation would also include the effectiveness of providing avenues of private communications by donors to indicate whether or not their blood should be used for transfusions.

Second would be an evaluation of whether or not exclusion of gay males has in fact resulted in a reduction of blood-transmitted cases of AIDS. The time between transfusion and onset of illness has ranged from 10 to 43 months, with an average of about 24 months (143). Cases of blood-transmitted AIDS that were diagnosed through the end of 1984, would have resulted from transfusions of blood which were donated prior to instituting the donor exclusion policies, which began in early 1983. If donor exclusion policies have made a difference, the effect should not begin to appear until late 1984.

These evaluations could also be tied to the expected development of highly specific laboratory tests for AIDS. As those expected tests are instituted and evaluated, a reassessment of current donor screening policies could help determine whether or not they should continue, be modified, or be eliminated.

These evaluations were discussed at the February 1984 meeting of blood bankers convened by CDC, but no decisions were made. CDC sees its primary role as risk assessment, not risk management. Therefore, thought was given to the role of the blood banking organizations in the evaluation of donor screening.

Individual blood centers have instituted variations on the basic donor screening recommendations, such as different ways to allow donors to withdraw their donations in private. Several of these centers have ongoing evaluations of these efforts, and the blood organizations (AABB, ARC, CCBC) could coordinate these efforts or mount a centralized research effort. Thus, ***blood organizations could be encouraged to conduct evaluations of donor screening and its impact on blood-transmitted AIDS.***

The alternative to a blood banking organization-directed evaluation is to direct Federal agencies to evaluate donor screening and its impact on blood-transmitted AIDS. Federal agencies could play the primary role in evaluating donor screening, with cooperation and/or contracting with the voluntary organizations or directly with a consortium of blood centers to perform the actual study. A possible locus for this Federal role could be the National Center for Health Services Research instead of CDC, NIH, or FDA, since the latter agencies are oriented more toward epidemiological field work and basic and applied biomedical research. It is conceivable that FDA could sponsor the evaluation because of its regulatory responsibilities.

Congress could advise the Department of Health and Human Services as to its priorities in this evaluation as against other evaluations of blood-transmitted AIDS, or it could provide separate funds. The evaluation could also be expanded to address the broader question of the continued need for donor screening methods specific to AIDS once a specific laboratory test for AIDS is in place.

Identification of Suspected AIDS-Carrying Donors and Recipients of Their Blood Donations.—CDC ***has gathered and continues to accumulate information on AIDS cases in general and on donors who have been implicated with cases suspected to be blood transfusion related, although they are now doing so with a coded system, making donors anonymous even to CDC until tracing is required.*** While some health departments have a policy to inform the local blood center as new cases of AIDS are diagnosed in order to match their names with blood donor lists (e.g., the San Francisco health department and Irwin Memorial Blood Bank), blood donations are not necessarily limited to the current city of residence, particularly with the mobility associated with modern life. One issue, then, has been: ***should the names of AIDS patients be made available, to what extent, and to whom?*** For example, should all State health departments be notified? Should all blood banks be notified, so that they can match the list of names with their donor registries?

Finding donors who actually have had AIDS has been the exception. Most of the "suspected" donors have not been found to actually have AIDS; they either belong to a high-risk group (e.g., are gay males) or have nonspecific laboratory abnormalities (e.g., reversed T-lymphocyte helper: suppressor ratios) or physical signs that could be AIDS related (e.g., enlarged lymph nodes). The use of a test for HTLV-III will also identify persons who have been exposed to the presumed AIDS agent and who may or may not be carriers of the virus. ***Should these donors be treated in the same way as confirmed AIDS patients, insofar as releasing their names is concerned?***

An even more vexing problem has been in dealing with patients who received blood components from donors who are suspected in the blood-transfusion AIDS cases. Should they be told, or should that information be passed on only to the blood bank which provided the blood, or to the patient's personal physician, leaving it up to his/her judgment to inform the patient? Since ***monitoring of these recipients of suspected AIDS-contaminated blood is important in determining the epidemiological characteristics of the disease-e. g.,*** its rates of infectivity, morbidity, and mortality—it does not seem practical to design such monitoring activities without informing the patients.

These issues were addressed at the February 1984 CDC meeting, a subsequent March 1984 meeting of the National Heart, Lung, and Blood Institute's AIDS Working Group, and another meeting of the AIDS Working Group in late May 1984. This latter meeting also included medical ethicists to see how such studies could be reconciled with the ethical problems. A previous assessment of "Confidentiality in Research on AIDS" had been completed by The Hastings Center, but the focus of that assessment was on assuring the confidentiality of AIDS victims, and not to the issue above—i. e., how to approach the question of monitoring other recipients of suspected AIDS-contaminated blood, and who should be informed.

Laboratory Tests for AIDS.—Current ***surrogate tests lead to exclusion of far more donors than are ever expected to actually have or develop AIDS, and seem to have been instituted more to allay patients' and physicians' fears rather than in hopes of decreasing exposure to AIDS,*** Besides increasing costs due to the expense of testing, discarding of blood after collection, lost donors, and the need to recruit additional donors, the psychic costs to donors labeled as suspect have been subordinated in order to reduce the psychic costs of potential and actual recipients and their physicians. Given the public apprehension surrounding AIDS, this situation can be expected to continue. For example, testing for past infections with hepatitis B (anti-HBc) is expected to exclude about 6 percent of current voluntary donors and 15 percent of commercial source plasma donors, and apparently this cost is not viewed as too high for the psychic benefit it is expected to produce.

The criterion used in decisions to institute these programs appears to be whether the added costs can be handled, not whether in fact AIDS will be reduced. ***However, these decisions seem entirely compatible with public reaction to the threat*** of ***AIDS*** in the blood supply. The risk is very small, but the fear is great, ***and the perception*** that ***something is being done is important to public confidence.***

A highly accurate, AIDS-specific test should decrease the perceived need for adopting any of the surrogate tests that have been proposed, but reassuring the public will probably mean that these tests ***can also be expected to be applied far beyond the application that would be scientifically justified,*** For example, hepatitis B testing is justified on the basis of its incidence and severity, and the search for a test for non-A, non-B hepatitis is also justified on that basis. On the other hand, the continued requirement for testing for syphilis of all whole blood and plasma collections has been questioned because of its low cost effectiveness. The syphilis testing example, however, points to the fact that safety has been the primary concern, and it can be expected to take priority once an AIDS-specific test is available.

Thus, it can be expected that the test for HTLV-111 will be a requirement for all blood and plasma collections, regardless of the relative degree of risk among blood banks and geographic areas. Even if not required for all, blood banks and plasma collectors will feel compelled to perform the test anyway because of the public confidence factor and the threat of lawsuits. It should also be reasonable to expect that plasma fractionators, because of the pooling of plasma from thousands of donors, may be required to test for AIDS a second time when they receive plasma from blood banks and source plasma centers (this is currently being discussed in FDA for the test of active hepatitis B, the HBsAg test, which is currently required only at the time of donation).

Such additional testing will further raise the costs of blood and plasma products, but the advent of cost containment measures will exert pressures in the opposite direction; i.e., it can no longer be assumed that blood testing (and other processing) costs can be passed on to purchasers. The circumstances surrounding AIDS will most likely compel nationwide adoption of tests that are developed, ***but the additional costs of such testing should provide incentives to reassess all*** of ***the tests that have been adopted over the years to improve safety.*** Among these are the requirements for syphilis testing and for blood typing each time a donor gives blood (blood types do not change).

Directed Donations.—Interest in directed donations increased with AIDS and has been implemented in some of the areas with a high incidence of AIDS (e.g., Los Angeles, San Francisco). Such interest may diminish with the availability of an accurate and sensitive test for AIDS, but individual blood centers-may maintain directed donations for individual patients indefinitely. A serious problem may arise, however, if ***organizations press for directed donations.*** In this case, ***entire sets*** of ***blood might be tied up and have the potential for disrupting the present, well-balanced system of blood supplies. The potential scope is great: a third of those who donate regularly do so to contribute to a company blood drive*** (25).

Costs of Blood Products

Charges for blood products vary considerably but are generally not considered to be a national problem because they account for only about 1 percent of total health care costs and because increases in charges do not appear to have exceeded increases in overall health care costs. However, the costs of blood products may cause hardships for two types of consumers: hemophiliacs and public hospitals.

Points to Consider

Coverage for Hemophiliacs' Care .—The situation for hemophiliacs has improved dramatically

since passage of Public Law 94-63 in 1975. The law provided funding for the creation of comprehensive hemophilia treatment centers, 23 of which have since been created. A recent survey of about half of those centers found that conditions had markedly improved for the 3,705 patients seen in the fifth year of the program. Compared to the year before the programs had started, the costs of total care, including rates of hospitalization, had been reduced, and unemployment among hemophiliacs was lower. The proportion of patients with third-party coverage had also grown, both because employment of hemophiliacs increased as a result of better treatment, and because health care workers at the centers have helped patients arrange for coverage. However, the survey of treatment centers represented only those hemophiliacs with access to comprehensive treatment centers, probably half of the hemophiliac population. In addition, third-party payments may not cover the plasma derivatives needed for prophylactic treatment, which can cost $13,000 per year for a severe hemophiliac.

Medicare does not, and private insurers often do not, cover the costs of the needed blood products on an outpatient basis, because plasma derivatives are considered to be pharmaceuticals. Distributors of coagulation proteins sometimes disregard copayment requirements for their hemophiliac clients. Coverage is further complicated by the fact that unlike the End-Stage Renal Disease Program under Medicare, which recognizes patients with end-stage renal disease as being totally disabled and thus eligible for Medicare coverage for dialysis and transplants, hemophiliacs can receive Medicare coverage only through a case-by-case determination. State plans to cover hemophiliacs exist but vary widely in comprehensiveness, and hemophiliacs have been known to relocate in search of better benefits, disassociating themselves from important family and community ties. Thus, ***opportunities exist for improving health care provisions for hemophiliacs,*** if ***not by creating a special program for them, then by providing coverage for blood products on an outpatient basis.***

Costs of Blood for Public Hospitals.—As for many other products and services the purchase of blood is a problem for public hospitals. Blood centers feel obliged to deliver needed blood products to public hospitals regardless of the fact that they may not be paid, and public hospital bills are often written off as uncollectible (420). Thus, the costs of blood for public hospitals are partially underwritten by hospitals which can pay the prices that blood centers charge. This situation is somewhat analogous to the sources and users of blood itself-suburban, rural, and middle-class urban residents already support inner cities by providing much of the needed blood. ***As cost containment measures pressure hospitals to reduce overall per patient costs, pressure on blood centers to lower or not increase their charges may make it difficult for them to continue absorbing losses from their public hospital clients.***

Containment of Health Care Costs

The diagnosis-related grouping (DRG) method of payment for Medicare is now in the process of implementation. Under previous cost reimbursement, there were few incentives for hospitals to be price-conscious in purchasing blood products, reliability of sources being their primary criterion.

Higher charges for whole blood and red cells were associated with hospitals that collect part of their blood requirements v. those hospitals that did not (576). While no comparable hospital blood bank cost data were available, it seems reasonable to assume that at least part of the higher charges was due to higher costs. For example, regional blood centers have been found to have economies of scale for total costs. Under cost reimbursement, there was no incentive for hospitals to rely more on regional blood centers, but under fixed reimbursement rates management will have to reassess its arrangements for blood supplies. Even for hospital blood banks with costs lower than those of regional blood centers, other factors may lead to greater dependence on the regional center. These include the possibility of duplication of services, competition for blood

donors, inventory control and outdating, and greater need for blood because of expanded and new services (189).

Another factor is the trend in ownership in both for-profit and nonprofit hospitals toward multi-hospital chains, which are introducing corporate management practices and volume purchases, thereby inserting hospital management more into the traditional relationships between hospital blood banks / transfusion services and regional blood centers. These developments mean that hospital management will be taking a close look at the cost effectiveness of purchasing blood from regional centers versus maintaining complete blood banking operations, although it has been argued that because blood is such a small portion of a patient's bill, such reviews may not occur for some time (534).

However, a move toward greater dependence on regional centers maybe tempered by the need to generate income to support remaining blood banking activities. For example, with a fixed overhead in running hospital blood banks, hospitals may look toward additional services to generate income, such as platelet collections and therapeutic apheresis. Another opinion is that it is more cost effective for hospitals to collect their own blood, but that it has been more convenient to purchase it from a blood center (140).

Finally, one blood banker predicted that blood centers would expand even more and hospital blood banks would eventually close. The blood center has freedom from hospital cost control, and has a distinct advantage when it comes to research opportunities, since the blood center does not have the external controls that are found in hospitals (90).

Clearly, what will actually happen is still quite speculative, but some indications of the influence of cost containment measures are beginning to emerge. Limits were placed on hospital payment rates to provide them with incentives to be cost-conscious, including not only the services they performed, but also the purchases they made. While capital costs have been excluded from the DRG payment system by the current legislation, purchases of supplies have not. One blood center has been told by one of its hospitals that it would not accept any price increases in 1984 (196). In addition, the president of the ABC has expressed concern that hospitals ***are now*** shopping around for blood supplies on the basis of price, even using the AABB Clearinghouse at times in preference to their usual regional blood center sources (383).

Points to Consider

Financing of Blood Center Operations .-Blood centers use their revenues for their operating, research, and capital costs. Predictability of demand (and related revenues) for their products has been made easier by the regional systems that have developed over the past decade. Ad hoc and formal sharing of blood between blood centers with shortages and surpluses have also contributed to a fairly predictable stream of revenue. Furthermore, as availability / convenience has been the controlling factor instead of price under previous cost reimbursement for hospital services, the prices that blood centers have quoted have generally been what they received.

Some price competition is now appearing for blood products, either through requests to hold prices level or through purchases from less expensive sources. ***Some blood bankers have already suggested that the service (processing)*** fee ***be treated as a pass-through, leaving under DRGs those costs of typing patients, cross-matching and all of the other services provided by the hospital for the patient (120).*** Whatever the merits of such a proposal, it is premature at this point. Very good reasons would have to be provided without opening the door for other health care sectors to clamor for such an exclusion. This does not mean, however, that these concerns should be dismissed. ***One area of concern is the research and training programs conducted by blood centers, and capital costs for new or improved facilities.*** The Red Cross, because of the large reserves it has accumulated from blood revenues, could help some of its centers to maintain their research and training programs, but independent blood centers do not have this cushion to fall back on.

One reason for proceeding with caution before reaching the conclusion that cost restraints will significantly affect the present supply system ***is the underlying assumption that price competition will (or could) develop into a significant purchasing*** factor. The system is, after all, based on a system of voluntary donations. While regions with surpluses and those with shortages are part of the system, and spot purchases at better prices than available at the regional blood center may occur, ***competitive purchases in the kinds of volumes that would endanger a*** region's ***blood center*** are not ***highly probable.*** In order to do so, competing blood centers and blood banks may have to collect blood far beyond their needs and would have to justify to their donors why they are doing so. Increased revenues would hardly be accepted as a valid reason. Thus, hospitals may augment their major purchases by "spot buying" on the basis of price, and the real impact on blood centers may be to make them more cost conscious in their operations.

Current Supply and Distribution **Systems.—The** same considerations apply to the effect of cost containment measures on the collection and distribution systems that have been nurtured over the past decade, with the blood center at the hub (regionalization). If ***publicized, overcollection of blood for the purpose of increasing revenues would threaten the blood center/donor relationship. As long as voluntary donors are the*** basic ***source of blood components, collection centers should not be able to increase their supplies for the purpose of competing for sales outside their existing distribution channels without threatening the relationship that has been so carefully nurtured over the years.*** Thus, current indications of price shopping may be a temporary phenomenon, or an activity that will continue only at the margin.

Alternatives and Substitutes for Blood Products

Recent advances in biotechnology, particularly in the field of recombinant DNA technology, have suddenly raised the prospect that alternative sources for some blood products can be available by the end of the 1980s. The gene for albumin was cloned a few years ago, and many recombinant DNA companies have publicly claimed to have both recombinant yeast and bacterial strains carrying the human albumin gene. Most companies appear to have this project on hold for the present, due to problems of scaleup to mass production, purification of the resulting product, and questions over whether a recombinant albumin could be priced competitively with albumin from human sources. Many of the technical problems facing commercialization of recombinant albumin are unique. Not until those problems are solved will recombinant albumin be capable of meeting worldwide demand for albumin.

Developing recombinant DNA sources for Factor VIII was initially a much more difficult process, because the protein is much larger than albumin, and bacteria are incapable of producing the entire molecule because of the complexity of the gene. One company (Genetics Institute) announced in December 1983 that it had cloned part of the gene for Factor VIII, and several other companies have given the impression that they were close to testing recombinant Factor VIII in clinical trials.

These claims were met with skepticism, given the complexity of the molecule and its gene, and the instability of the biologically active protein. However, in April 1984, Genentech announced that it had succeeded in cloning the entire Factor VIII gene, and used a mammalian cell to produce the protein, thereby bypassing many of the problems inherent with bacteria or yeast as the cellular host. Genentech also claimed that it had tested the product and found it biologically active. Thus, technologies for producing both albumin and Factor VIII, the foundations of the plasma derivatives industry, are rapidly being developed. There are, however, some hurdles to be overcome before these products will be commercially available. These include development of techniques for production on a commercial scale, completion of tests of safety and efficacy, and approval by FDA for marketing. There is also the danger that litigation to resolve patent disputes maybe quite protracted, delaying commercial availability of new products until claims of priority are resolved.

Other potentially useful plasma proteins not presently produced by the plasma derivatives industry or produced only on a small scale are also under exploration or testing by recombinant DNA companies. However, the activities necessary for developing other useful protein products are different from those used to develop Factor VIII and albumin. Small markets, and the unexplored clinical utility of these proteins, may mean that companies will not devote resources to their development.

True cellular substitutes for blood are much further away. Two products, perfluorochemicals and hemoglobin solutions, have been under development for a number of years, but still face safety and efficacy hurdles before they will become available. Even if and when they do become available, however, they will not be true substitutes for red blood cells, but will be only partial substitutes which can be used in place of red cells in special circumstances. Platelet substitutes are much further away, although there is growing interest in this field. White blood cell substitutes do not seem to be needed, given the doubtful need for them now from human blood.

The approach of developing cellular substitutes on a synthetic basis maybe ultimately supplanted by cell culture techniques. Both red cells and platelets come from common progenitor "stem" cells found in bone marrow (and a small amount circulating in blood). If cell lines could be developed which both proliferate in massive amounts and can be controlled to differentiate into the desired cell types (red cells and platelets), a true alternative source of blood cells will have been accomplished. Given the rapid advances in cell culture techniques (e.g., hybridoma technology for the production of monoclinal antibodies) and understanding of cellular functions, it is not science fiction to assume that production of red blood cells and platelets from "stem" cells will eventually become a reality.

Nearly all of the work on developing recombinant DNA sources of plasma proteins is being conducted by biotechnology companies, some in conjunction with the parent corporations of the large fractionators of plasma (e.g., Green Cross of Japan, Baxter-Travenol). Most of the work on (partial) red cell substitutes has been performed by academic investigators or at military research institutes, although an array of commercial organizations has also been interested, ranging from plasma fractionation companies and large industrial concerns to small biotechnology firms. Most of the work on hemoglobin solutions has been sponsored by the military in its search for a battlefield resuscitation fluid. The company most closely associated with the other major class of partial red cell substitutes, perfluorochemicals, is Green Cross of Japan and its American subsidiary, Alpha Therapeutics (purchased a few years ago by Green Cross, and one of the four major plasma fractionators in the United States).

Points to Consider

Impact on the Plasma Derivatives Industry.—As an industry whose primary products are Factor VIII and albumin, the ***plasma derivatives sector is obviously vulnerable to inroads or eventual takeover*** of ***the market by recombinant DNA sources of the two principal plasma proteins that are marketed. Moreover, monoclinal antibodies may also replace the third principal part*** of ***the plasma derivatives market, the immune globulins.*** In the past few years, the plasma derivatives market has shifted more toward collection of antibodies toward specific diseases, collectively known as the "hyperimmune" globulins. Monoclonal antibodies would be more effective than even these hyperimmune globulins, because they would be composed of single antibodies, not a mixture with a high titer of one antibody as is the case for plasma from sensitized donors.

The large plasma fractionators have been positioning themselves so they will be able to switch to the new sources of plasma proteins, and it is likely that they will continue to be the major producers, or at least continue as the major marketers, of these new sources of plasma proteins. However, ***some destabilization of the plasma derivatives industry is inevitable, with possible difficulties in providing other, less profitable, derivatives such as Factor IX Complex.*** Source plasma centers are especially vulnerable, since their sole role is in providing the raw material, human plasma, from which current plasma pro-

teins are extracted. While the upshot for albumin may be a desired decline in its use because of questions of its appropriateness, there is some concern about how Factor IX will be provided to the relatively small population that needs it. In addition, the clinical utility of other plasma proteins may be harder to explore. Factor IX, for example, was "discovered" in the process of fractionating plasma for Factor VIII.

When and how this impact on plasma collectors and fractionation products will occur is not predictable at this time, although some impact seems inevitable. Even if recombinant DNA and monoclinal antibody sources of plasma proteins are phased in gradually, there could be large dislocations in the plasma derivatives industry. Many source plasma collection centers and some fractionation plants could close. The price and perhaps even availability of some of the plasma proteins would also be affected, not only because of competition from alternative sources, but also because of the nature of the processes in the plasma derivatives industry where the extraction of marketable proteins from plasma is done in successive steps, linking the costs of each plasma fraction product to the costs of the others.

Impact on the Voluntary Whole Blood Sector.—The voluntary sector could also experience negative consequences as a result of shifting plasma protein production to nonhuman sources. ***The whole blood and plasma sectors are now interrelated*** to a significant extent because of excess plasma capacity in whole blood collections, which has been sold to plasma fractionators or converted to plasma derivatives independently (New York Blood Center) or by contract (Red Cross). This interrelationship is ***a direct consequence of the increased*** volume of whole ***blood*** that has ***been separated into components over the past decade.*** Currently, the voluntary sector accounts for about 20 percent of the plasma derivatives market, and significant revenues would be lost. Possible consequences are increased prices for blood components because of lost income from plasma sales; increased collection of specific components (i.e., red cells, platelets), or at least attempts to make component-specific collections more cost effective; and increased transfusion therapy activities by blood centers to generate other sources of revenues.

Impact on Consumers.—Development of alternatives to human blood products has both positive and negative implications for consumers, particularly hemophiliacs. While recombinant antihemophilic factor (and other nonhuman-derived products) would be free of infectious agents, nonhuman alternatives will be more expensive, at least in the short run. In addition, less ***profitable products*** such as Factor IX Complex ***may not be produced, or may become exorbitantly expensive, and the clinical utility of trace proteins may not be explored by commercial firms.*** Thus, additional public support for hemophiliacs and for research on trace proteins in plasma may be necessary.

Appropriate Use

There is wide agreement that blood products are overused, but little data exist by which to evaluate the extent of overuse, in many cases because scientific precision is lacking as to when a component or derivative should be administered. Estimates of the extent of overuse are high: 20 to 25 percent for red blood cells (204), as much as 90 percent for albumin (8), and 95 percent for fresh-frozen plasma (457).

Initially, the focus was on the use of whole blood instead of red cell concentrates. Currently, questions continue on overuse of red cells and have focused especially on albumin, and fresh-frozen, single-donor plasma.

One of the most controversial areas concerning red cells is the matter of the "transfusion trigger," the hemoglobin level which is considered the point at which transfusion is required. For example, women naturally have lower hematocrits than men, but surgeons use the same support and ceiling hematocrit levels to indicate transfusions for both sexes. Iron-deficiency anemia continues to be among the leading reasons for transfusions (202), even though it rarely warrants transfusions.

The dramatic increase in the use of fresh-frozen plasma over the last decade has led to concerns that its uses are often vague and without scientific basis and that other products are available that are as effective and safer (567).

Even the growing use of platelets has been questioned; for example, their prophylactic use in pa-

tients with malignancies (see, e.g., 481), the practice of treating the "platelet count" rather than the patient, and the use of pheresis platelets over platelet concentrates.

Despite workshops and the development of guidelines for albumin use in the mid to late 1970s, its use continues and production continues to increase. Per capita use of albumin differs markedly from country to country, even in countries similar in levels of medical sophistication (388).

A key element of inappropriate use is that criteria for clinical use are often unclear. Past attempts to change medical practice in this area have been largely educational, using such methods as seminars, handbooks of suggested practices, and textbooks. These attempts appear to have been largely unsuccessful, although systematic data on specific uses of blood products are lacking.

Points to Consider

Direct Attempts to Improve Use.—The NHLBI's Division of Blood Diseases and Resources has instituted a program of "Transfusion Medicine Academic Awards" through which recipients will work with medical schools to incorporate transfusion medicine into the curriculum. Thus, ***one method is to build up a specialty base in transfusion medicine,***

Some blood centers have attempted to modify the practices of physicians directly. For example, at Puget Sound Blood Center in Seattle, requests for more than eight units of a blood component must be cleared through a blood center consultant before the blood is released. This is made possible because Puget Sound maintains a central crosshatching laboratory, and all orders for blood and blood products are received and reviewed in that lab. Most blood centers supply blood in volume to hospitals and are not aware of individual clinical practices. Thus, ***another method is for blood centers to have more control over the use of their products.***

A third method is to monitor use through hospital transfusion committees and pharmacy committees (for plasma derivatives), but such committees have been largely regarded as ineffective.

Indirect Effects on Improved Use. —The threat of AIDS has made patients and their physicians more cautious in their use of blood products, and perhaps this effect will outlive the current threat. A more sustained limiting factor, however, is the widely accepted need to curb health care costs and the implementation of the prospective payment diagnosis-related grouping system for Medicare that was recently enacted. ***The prospective payment method is likely to have the effect*** of ***revitalizing hospital transfusion and pharmacy committees' monitoring*** of physicians' use of blood products in attempts to stay within the limits of payments on a DRG basis.

Coordination of Blood Resources

Regionalization is not acknowledged by all to be the best approach to managing blood supplies, and a recurring question 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. 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 acceptable products at a sufficient level, or is there a better organizational framework for provision of blood at lower cost?

The need for resource sharing, on the other hand, is not seriously debated. 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. Without a single 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 AABB or ARC, as well as within them. In some regions, there are even local clearinghouses which serve functions similar to the AABB.

Other issues concerning coordination of blood resources revolve around the need for a blood

credit system, and the need for the American Blood Commission or some similar organization.

Points to Consider

Regionalization. —As discussed previously under cost containment, there are some indications that hospitals are shopping around for blood products on the basis of price, going outside their usual suppliers and even using the AABB Clearinghouse. Some blood bankers are concerned enough that they have suggested that the service (processing) fee for blood from blood banks be treated as a cost pass-through. However, the observation was made that it is hard to see how blood centers could explain to their donors why they should greatly increase their sales to hospitals outside their normal distribution channels, and why therefore donations should also greatly increase. Thus, sales of excess capacity could be justified, but increasing capacity in the face of existing surpluses would be hard to explain to the blood center's donors, assuming that blood center donors (or community representatives) are kept informed of the disposition of the blood they donate.

Sharing and the Blood Credit System.—One ***interesting aspect*** of ***AABB's Clearinghouse is that the blood credit/replacement system is alive and well, at least among blood banks, and to a lesser extent, for individuals.*** In addition to coordinating the movement of blood and blood components, the Clearinghouse transfers credits between blood banks and between regions where such programs exist. In 1983, 47 percent of the transactions coordinated by the Clearinghouse were for actual shipments of blood, including blood shipped for replacement. The remaining transactions consisted of issuing and/or transferring blood credits (25 percent) and payment of nonreplacement fees (28 percent). 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. ***The American Red Cross may not want to be involved in a single resource sharing system because it would mean participating in the AABB's system, which, although only partially, involves a credit system. The*** American Red Cross withdrew from the AABB Clearinghouse in 1976 in an attempt to put more fully into practice its philosophy of "community responsibility."

Cost-consciousness on the part of corporations, many of whom are beginning to self-insure for health care because of rising costs over the past decade, and the costs that they incur for company-sponsored blood drives which are usually conducted during business hours, may combine to provide a continued stimulus for these corporations to maintain the blood credit system. Thus, it is not unreasonable to ask whether or not ***cost-consciousness may lead to increased demand for*** a ***blood credit system or for discounts on blood costs, such as on processing*** fees. Over the past 10 years, the use of blood credits has declined, but an increase in their use is obviously not viewed negatively by all. Payment of the nonreplacement fee goes to the blood bank, not to any donor, and would be a welcome source of income. Donors only benefit when they or their immediate families are treated in a hospital which is part of a credit system, usually within a year of the donation.

Discounts on processing fees, instead of maintenance/revival of a nonreplacement fee, would benefit transfusion recipients directly, if only modestly. However, there is a wide array of health insurance plans, and they treat blood costs in a variety of ways. Patients would directly benefit only if such costs were part of their deductible or coinsurance requirements. Moreover, administration of such a discount system could be extremely complex. The blood credit system can result in lack of coordination for individual patients who give blood at a center where no credits are given, yet who receive transfusions at hospitals where replacement fees are charged. It ***may be necessary for the blood banking community to take a stand on whether blood credits should increase again, or conflict between the representative organizations may be renewed,***

American Blood Commission. —The impact of the American Blood Commission on coordination of blood resources is difficult to evaluate. ABC was unable, for example, to get the blood collecting organizations to take a unified stand on the

blood credit system, or to finalize a single resource sharing agreement. Similarly, its attempt at establishing a National Blood Data Center met with mixed reviews. However, many credit it with reducing the conflict between the AABB and ARC which 10 years ago threatened to lead to Federal takeover of blood collection and distribution. ABC today receives no Federal funds, and is dependent on member fees and private donations. Both membership and private donations have recently declined, leaving ABC facing an annual deficit for the first time since its inception. It is ***not clear what could be done to stabilize ABC, but many believe its demise would mean the attenuation of constructive dialog between the blood collecting organizations.***

Voluntary v. Commercial

A continuing issue in the use of blood-derived products is that of voluntary v. commercial sources. This was a critical issue in the whole blood sector a decade ago, with the result that commercial whole blood collections have been effectively eliminated. Currently, the distinction between voluntary and paid whole blood donations has been maintained through the labeling of blood components as being derived from a "paid donor" or "voluntary donor. " This labeling is applicable to whole blood, red cells, platelets, single donor plasma, and cryoprecipitate, but does not apply to source plasma or plasma derivatives. Donor and laboratory screening tests have been applied over the last decade, with the result that there are no substantial differences in the safety of plasma derivatives whether they are derived from voluntary or commercial sources. One reason is the necessary pooling of large amounts of plasma from individual donors for the efficient processing of plasma into plasma derivatives.

But the availability of products that are derived from human tissues may also be influenced by criteria other than whether or not the market has resulted in a safe, readily available product. Canada, for example, in 1980, amended its national policy of a voluntary blood supply by extending its nonprofit policy to fractionation products. Currently, the only major import is Factor VIII, at the rate of 20 million to 22 million activity units per year. Other products imported in relatively small amounts are specific immunoglobulins to varicella zoster, hepatitis B, tetanus and rabies, and the activated Factor IX Complex. Canadian Red Cross (CRC) meets all requirements for blood and blood components, and CRC plasma sources supply all albumin, normal Factor IX Complex, pooled immune serum globulins, and about 20 million activity units of Factor VIII. Canada also has developed a collection system oriented toward maximum preservation of plasma coagulation proteins so that 95 percent of its whole blood collections can be processed and the plasma frozen within 12 hours (147).

The Canadian experience shows that a voluntary system can meet nearly all blood needs, but other factors make it unlikely that a policy will be pursued in the United States to make the voluntary sector the exclusive or even dominant collector of plasma as well as whole blood.

Points to Consider

Can the Voluntary Sector Provide All Blood Products?—It has been estimated that voluntary whole blood collections would have to triple to meet U.S. production of plasma derivatives (165). U.S. plasma sources, however, also supply a large part of the world market, and not as much plasma would be needed to supply the U.S. market alone. But sales abroad have been claimed to help to lower prices in the United States, whatever one's position is on the morality of this situation.

Whether the voluntary sector would want the responsibility of serving the United States and part of the world markets then becomes the question. Aside from the problems of establishing and maintaining an adequate donor base, costs for starting up or retooling plasma fractionation plants are substantial.

New technologies make the future prospects of the plasma derivatives industry sufficiently doubtful that no planned movement toward a voluntary system can be expected. ***By the end of the century, there is a real chance that plasma as a source of current biological proteins will be replaced by recombinant DNA and monoclinal antibody technologies.*** For the first time, there are

real prospects that the longstanding controversy ***over commercial plasma donors may be solved—not through implementation of a deliberate, contested public policy, but through advances in technology which could make*** the voluntary *v.* com***mercial policy debate moot.***

Blood centers themselves do not see the plasma sector as their future, but are instead looking toward organ and tissue banking and their related technologies, such as tissue typing, as their growth areas.

CONCLUSION

The past decade has been a contentious one for the blood resources community, but the results have been generally gratifying, and the blood community's internal conflicts have generally been out of the public's eye— perhaps indicating public satisfaction with and commitment to the informal system even while internal battles continued.

The "National Blood Policy" which has guided development of our blood services complex over the past decade was not codified in law but was an expression of commitment, backed by specific activities that used the Policy as a general guiding principle. The establishment of a Blood Program in the National Heart, Lung, and Blood Institute, represented by the NHLBI's Division of Blood Diseases and Resources, and the strengthening of safety and efficacy standards through establishment of a blood products division in the Office of Biologics Research and Review (previously the Bureau of Biologics) provided the primary instruments through which Federal policy could be formulated, implemented, and maintained. In the initial years of the NBP, there was a direct fiscal relationship between the Federal and private sectors through major support of the private sector body, the American Blood Commission, which was established in order to provide for continued, decentralized management of blood resources. Federal interest at the central policy level within the Department of Health and Human Services slowly faded away, leaving the Blood Division at NHLBI and the Office of Biologics Research and Review as the primary Federal participants in continuing with the objectives of the National Blood Policy, and improving the biomedical base of blood resources and the safety and effectiveness of blood products.

OTA concludes from this broad review of blood policy and technology that the policies implemented over the past decade have been successful in assuring a safe and available blood supply, This has occurred despite continuing internal conflicts; e.g., whether or not to maintain a credit system, other differences between the major organizations involved in blood collection, and commercial v. nonprofit operations. Conflicts of these types seem inevitable in the pluralistic system which evolved, should not come as a surprise, and should not be the basis for judging whether or not the policies of the past decade have been successful.

The current situation presents new challenges, AIDS has shaken the public's confidence in blood supplies far beyond its actual risk to blood recipients, yet no widespread shortages have resulted, and both donors and blood collection organizations have generally responded to the challenge. It remains to be seen if AIDS will have a long-lasting effect on blood resources. In addition, blood suppliers and users face additional pressures because of continually escalating health care costs and recent economic policies instituted to deal with them. And on top of all of this, truly new technologies have emerged which have a high probability of replacing some blood products by the end of the 1980s, and if not yet making human-derived blood products obsolete, represent the first real steps toward that event.

Given the overall success of the past decade and the transitional nature of present circumstances, the prudent course would be to continue with the cooperative arrangements that have been estab***lished over the past years and to monitor key developments to anticipate when particular adjust-***

ments need to be made. In the previous section, OTA has identified what it considers as the key issues and enumerated some of the points that need to be considered in determining future actions in these issue areas. The following chapters provide background information and more detailed discussions of these and related issues.

Some of these issues involve actions in which the Federal Government is expected to take the leading role, such as in assurances of safety, although the private sector is also deeply involved and needs and wants to participate in such actions. Other areas, such as use of the blood credit or nonreplacement fee, involve differences in philosophy about how much responsibility individuals should have in providing blood resources and what rewards they should have for doing so. ***Thus, Federal participation involves resolving or reconciling these differences among the different collection organizations and their clientele,*** should any decision be made to modify the course of developments in the blood field.

Still other areas involve consequences of Federal policies directed at even larger problems—the continually escalating costs of ***health care and recent legislation to "cap" these costs through prospective payment mechanisms—whose purpose*** was ***to impose exactly the kinds of cost-saving behavior which hospitals apparently are beginning to exhibit, and over which the blood community is so concerned.*** The architects of these broader policy changes in health care financing are aware of the negative consequences in particular circumstances—e. g., their effects on research and training programs and capital acquisitions. Such consequences also need to be explored in the blood resources area, but simply shielding blood products from these cost containment efforts is no answer. ***Federal action might also be considered in the areas of support for biomedical research and studies to determine appropriate use of blood products, and improved coverage for hemophiliacs.***

A decade ago, developing a data system for blood resources was a major objective of the National Blood Policy. The efforts subsequently undertaken under the sponsorship of the American Blood Commission and financed primarily by the Blood Resources Program at NHLBI did not meet expectations. In retrospect, one problem was the general nature of the data and the inability to find sponsors to ***continue*** the data collection. In other words, the data may have been informative and useful in understanding the general contours of the blood services complex, but they were not useful to organizations interested in information that could help them in their operations. Thus, there is general agreement that future data collections should be much more targeted.

The problem with collecting data which would be useful to the operations of organizations is the issue of who should be responsible for collecting it, and the relevance of those types of data for public policy illumination and formulation. Another problem is that, while specialized data sets are the most useful, they also tend to be fragmented, and some type of coordination needs to be arranged. For example, both the American Red Cross and members of the American Association of Blood Banks are involved in data collection on a daily basis, and much of this data would be useful for public policy purposes. In fact, much of this information is used for determining policy within those organizations, and the organizations are willing to share a large amount of this information, although as health care provision becomes more competitive as a consequence of cost containment efforts, much of this information is coming to be regarded as proprietary. Other information sources can be found in the data systems that are being organized to monitor the effects of the Medicare prospective payment system, which have the potential to provide more specific information on use and costs than have been possible previously.

Monitoring functions which include coordination of data sources require a capacity for sustained activities, and the problem is in identifying who can and should assume this function. The Federal Government's primary data collection organization in the health field, the ***National Center for Health Statistics,*** can collect comprehensive data on specific issues, but the kinds of data needed to help formulate policy in the issue areas identified above are of a different type. ***The National Center for Health Services Research*** can

also conduct policy-relevant research, but it too, lacks the capacity for sustained and coordinated activities. ***The Office of the Assistant Secretary for- Health*** is the logical choice for such data coordination and policy formulation, but it is preoccupied with immediate issues and functions more as the receiver rather than as the gatherer of information. ***FDA and NIH,*** which are the primary Federal agencies involved in blood resources on a sustained basis, could be given that responsibility, but their primary responsibilities are in circumscribed areas of the blood services area—assuring safety and efficacy and resource building—and the net effect would be what has happened in the past; i.e., they can be required to fund such activities, but would not be able to assume the primary Federal role in determining overall blood resources policy.

The private sector could conduct these activities, and in fact would argue that they are already doing much of it. Federal funds could again be provided, as it was for the data collection efforts and early general support of the American Blood Commission. Two problems would recur, however. First, is the question of whether any single private sector organization would be recognized by the diverse interests in the blood services complex as a legitimate policymaking body, instead of serving primarily as a policy debating forum. Second is the question of how sustainable Government funding could be.

If there are no obvious answers as to who could assume both a monitoring and policy formulation role, or on the even more limited role of monitoring developments in blood resources, perhaps a different approach should be taken. Just as the emphasis on data needs has shifted from the general to the specific, ***a more practical and useful approach might be to have periodic appraisals that monitor specific issues to see: 1) what happens in these issue areas over time, 2) whether the issues identified initially continue as the primary ones, and 3) what new issues arise.*** Thus, one approach is to formulate a set of questions and use them as guidelines for narrowing the issues, to see how these questions are resolved, and how public policy can contribute to their resolution. The issues and points to consider that have been enumerated above represent one attempt to delineate those questions, based on the broad overview represented by this report.

Certain policies could be extracted from this approach. For example, oversight ***hearings*** could be structured around the identified issues, with both private organizations and Federal agencies contributing information to further clarify the issues and to suggest approaches to their resolution. Periodic hearings or other methods of followup could then take place to follow the course of events. For example, ***the National Academy of Sciences could be requested to review these issues periodically,*** or ***the*** Federal ***Department*** of ***Health and Human Services could be required to reassess them in reports to Congress as is often required for other policy issues. Specific issues could be examined in detail by any of the congressional support agencies. A restatement of the National Blood Policy could also be constructed to provide general guidance—as its original formulation a decade ago has done. Within any of these approaches,*** specific actions ***could be taken as the need*** arises, ***either by legislative action, by administrative changes in the operations*** of ***Federal agencies, or by voluntary actions by the private sector.***

In conclusion, in the decade since the National Blood Policy was announced, blood resources have become safer and more available, despite continuing differences among participants in the blood services complex. This should not be surprising, given the decentralized, pluralistic approach that was continued under the NBP. Today, AIDS, cost-consciousness, and radically new technologies have significantly affected the blood services complex and portend changes that will most likely be even more significant. These changes are occurring rapidly; over the short time that this report was prepared, the cause of AIDS has been apparently identified and tests for its detection are under development, and the entire gene for Factor VIII has been cloned, adding to the already available gene for albumin.

The transition that the blood services complex is currently undergoing, as represented by these events, calls for a policy of focused monitoring and adjustments to particular circumstances as the