3.
The Blood Services Complex

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3. The Blood Services Complex

PART 1: THE VOLUNTARY, WHOLE BLOOD, AND BLOOD COMPONENTS SECTOR

Introduction

The whole blood sector is called "voluntary" because it collects blood primarily from unpaid donors. In 1980, only 2.2 percent of the 11,880,000 units of whole blood collected was collected from paid donors (518), in contrast to the situation of 10 years ago when over 10 percent of whole blood was collected commercially. 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. In addition, the voluntary sector depends on the commercial pharmaceutical firms to fractionate its recovered and salvaged plasma.

Community or regional blood centers generally provide a full range of blood services to a surrounding geographic area. These services may include collection, testing, and labeling of blood, and distribution of blood and blood products to hospitals, physicians, and hemophilia care centers. In addition, blood centers often conduct research and training programs.

Hospital blood banks generally provide a smaller range of services than regional blood centers, usually limited to the collection and storage of whole blood and components. Some common laboratory tests may be available in-house, depending on the size and scope of the blood bank operations, while other tests must be sent out to private laboratories or the regional blood center. Often hospital blood banks orient donor recruitment efforts to the friends and relatives of patients; thus, many of the existing nonreplacement fee programs are associated with hospital blood banks.

The third type of facility involved in the voluntary sector is the hospital transfusion service, which is responsible for the administration of blood and blood components within the hospital. Some hospitals do not collect any blood but obtain their blood and blood products through an outside supplier, either a regional blood center or another hospital blood bank, thus making the transfusion service the primary participant in blood management and use in such noncollecting hospitals. While transfusion services also serve as blood banks, they are called transfusion services to differentiate them from blood banks which collect, as well as store, blood.

Although blood collection began in hospital blood banks, over time they have ***come*** to play less of a role in blood collection. In 1971, 69 percent of the blood collected came from regional and community blood centers **(555).** By 1980, regional and community blood centers collected 88 percent of the total, and comparable, though less reliable figures for 1981 indicate that 91 percent of total whole blood collections were made through blood centers (29). Surgenor & Schnitzer / ABC (518) attribute the predominance of regional centers to the centers' ability to collect blood through constant mobile collections. In 1980, 69.5 percent of whole blood collections was through mobile units. There is some speculation that the dominance of regional blood centers may be reversed in the future as hospitals seek to gain control over costs in the face of such cost containment measures as the prospective payment system—although, as discussed below, there are those who argue that cost containment may accelerate the trend toward more centralized collections (see ch. 5, pt. 3).

Blood Collecting Organizations

As shown in figure 4 and table 10, blood collection and transfusion facilities in the voluntary sector are represented by three organizations with overlapping memberships: the American Red Cross (ARC), the American Association of Blood Banks (AABB), and the Council of Community Blood Centers (CCBC). The American Red Cross has 57 regional centers operating under a single Federal license, and also maintains an affiliation with the New York Blood Center (which is a member of CCBC). The Red Cross regional centers cover about half the geographic area of the United States, and collect about half the Nation's whole blood.

Another 45 percent of the Nation's whole blood is collected by institutional members of the American Association of Blood Banks, including members who belong to CCBC. In 1980, seven ARC regional centers and all but two Council of Community Blood Centers belonged to AABB, as did 1,977 blood collecting hospitals. There were 101 community blood centers that were members only of AABB. Approximately 2 percent of blood collections were through 16 unaffiliated blood centers.

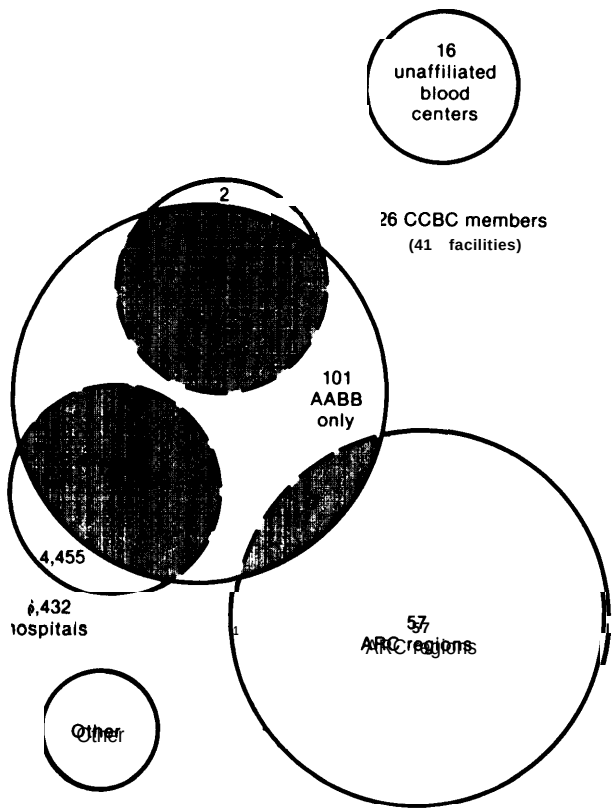
Table 10.—Whole Blood Collections by Type of Facility and Affiliation, 1980

	Number of facilities	Units collected
Regional and community blood centers:		
AABB only	101	2,163,614
CCBC	41a	1,866,586
ARC	57	5,434,783
Unaffiliated	16	208,421
Total for blood centers	215	9,673,404
Hospitals:		
AABB affiliated	1,977	1,116,143
Unaffiliated	4,455	73,895
Total for hospitals	6,432	1,190,038
Other collections		16,637
Total—U.S. collections		10,880,079
Euroblood imported		265,839
Grand total		11,145,918

[a]In 1980 26 CCBC members ran 41 blood collecting facilities.

SOURCE: Surgenor and Schnitzer/ABC, 1983.

Figure 4.—Relationships Among Blood Collecting Facilities, 1980[1]



[1]Size of circles represents approximate collection of whole blood in units (see fig. 8).

SOURCE: Surgenor and Schnitzer/ABC, 1983.

The AABB was formed in 1947 to protect the interests of already existing hospital blood banks in the face of a plan announced by the Red Cross to attempt to collect and organize the Nation's entire blood supply (307). Existing hospital and regional blood banks wanted to maintain their established collection programs. Today, the AABB represents over 2,000 institutional (voting) members, as well as about 7,000 individual members, primarily blood bank personnel (e.g., administrators, medical technologists). Institutional members include blood centers, hospital blood banks, and transfusion services. While blood centers account for two-thirds of the blood collected by AABB members (29), each institutional member has a single vote regardless of its size.

In 1962, the Council of Community Blood Centers was formed by six community blood bank administrators who were dissatisfied with the dominance of the AABB by hospital blood banks.

CCBC today consists of 27 institutional members, i.e., community or regional blood centers. All but two current CCBC members (New York Blood Center and Puget Sound Blood Center in Seattle) are also members of AABB. CCBC as an organization has played a relatively minor role in the politics of whole blood delivery, which has been dominated by ARC and AABB. CCBC'S recent move to the Washington, DC, area, where the Red Cross, the AABB, and the American Blood Commission are headquartered, was a move designed in part to make CCBC more of an active participant in National Blood Policy deliberations.

Thus, three major organizations represent almost all the blood collection organizations in the United States. Although there is some overlap in organizational membership and in function, the three major organizations espouse different philosophies and are designed to serve different functions (see table 11). The AABB and CCBC are organizations which represent individual blood collection facilities. The Red Cross, as a corporation and a blood collector in its own right, provides a Federal license to collect and process blood as well as an organizational framework to its member centers, although each center operates somewhat independently and is required to be more or less self-sufficient. "

American Red Cross (ARC) Blood Services

Red Cross chapters choose whether or not to engage in blood services and other services offered by the Red Cross, except disaster services and services to the Armed Forces, which are required to be available from all chapters. In 1982, 1,873 of the 3,01.1 Red Cross chapters participated in 57 ARC regional blood services. Donor recruitment, blood collection, and processing are performed by volunteers and staff of the regional centers. In addition to blood collection, regional centers also provide diagnostic and other blood-related services. National headquarters provides standards for its 57 regional blood centers and inspects them periodically. Interregional resource sharing is accomplished by the use of a computerized inventory system. ARC national also maintains a Rare Donor Registry, and many of its regions conduct research (so).

Table II.—Activities of Three Major Voluntary Blood Service Organizations

	ARC	AABB	CCBC
Actual blood services:			
Number of institutional members	57 regions 1,873 chapters	2,176	27
Units of blood collected by organization or members in 1981[a]	5,799,024	3,395,854[b]	2,320,750[c]
Actual blood collection	x	•	•
Formal resource sharing program	x	x	
Other ***activities*** *or characteristics:*			
Management conferences	x	x	x
Government liaison	x	x	x
Organ and tissue procurement	x	•*	•*
Scientific programs	x	x	
Scientific and educational publications	x	x	
Rare donor registry	x	x	
Blood bank procedures manual	x	x	
Standards published	x	x	
Institutional inspection and accreditation	x	x	
Training for technologies	x	x	
Incorporation as single entity	x		
Plasma products marketed	x		
Formal ongoing strategic planning activity	x		

• Collected by members.
* "Several members of these organizations are engaged in organ and tissue procurement.
[a]Source: AABB, untitled, 1983.
[b]Excludes amount collected by the 24 CCBC members and 7 ARC regions who are also AABB members.
[c]Excludes Euroblood.
[d]AABB publishes standards for the industry. ARC publishes standards which are used internally; however, these have been cited in court cases as the basis for standards of care.

SOURCE: Office of Technology Assessment.

Red Cross Blood Services also maintains a plasma products division operating out of its national headquarters, which is responsible for arranging contracts for fractionation of plasma from Red Cross blood collections and marketing of the products on a competitive basis with the commercial fractionation industry (see below). The Red Cross recently entered into an agreement with Baxter-Travenol which would give it more control over fractionation of the plasma it collects (and the ability to develop new products), but Red Cross does not fractionate its own plasma. In general, **85** percent of the plasma products sold by the Red Cross (primarily albumin and Factor VIII) is marketed by and within Red Cross regions; and the remaining 15 percent is marketed outside the regions (486). Eleven Red Cross regions are also licensed as source plasma centers.

Other fairly new activities of the Red Cross include efforts at strategic planning and management, and involvement in organ and tissue procurement (see ch. 7, pt. 2). In the last year, Red Cross Blood Services has created a Planning, Marketing, and Operations Research Division at National Headquarters. Blood services is one concern of an organization-wide planning group called the President's Council. The Red Cross is concerned that particularly because of technological advances such as genetic engineering, blood services as it exists today may be a declining industry. Currently, Blood Services accounts for almost 60 percent of the Red Cross's gross revenues (see "Costs and Charges for Blood Products" for further discussion of Red Cross Blood Services finances).

The entire ARC organization holds a special position in the national blood services complex. ARC is the only one of the blood service organizations with a congressional charter, although the charter is for disaster relief, not blood collections. (The charter is dated 1905, and Red Cross blood collections were not begun until the 1940s.) The President of the United States is ARC's honorary chair, and other cabinet members serve as honorary counselor and treasurer. The President appoints eight of the ARC's Board of Governors, and by an act of Congress ARC audit reports are reviewed by the Department of Defense. For these reasons, ARC is sometimes described as a quasi-governmental agency.

American Association of Blood Banks (AABB)

The American Association of Blood Banks characterizes itself as the only organization devoted exclusively to blood banking and blood transfusion services (28). As a scientific and administrative association, AABB sets technical standards which are followed by its members (see, e.g., 583), inspects and certifies the operations of its institutional members, and serves as a liaison with the Federal Government and with the other blood collection organizations. A major part of AABB's operation is its National and Regional Clearinghouse (see "Coordination of Blood Resources" in ch. 5), which accounted for two-thirds of its assets at the end of 1982 ($1.3 million of AABB's $2 million total) (20).

The basic standards in blood banking were first formalized and published by the AABB. The Red Cross and AABB have agreed to keep their standards essentially identical and even jointly publish the "Circular of Information" which must be included with shipments of blood components as required by the Food and Drug Administration (FDA). The AABB also initiated the first formal nongovernment inspection and accreditation system. All institutional members of AABB are inspected on a regular basis and are dropped from membership if they are not in compliance. AABB also conducts inspections of approved schools for training specialists in blood banking to ensure that the required educational standards are maintained.

Council of Community Blood Centers (CCBC)

The primary audience for CCBC activities is blood center managers. (The AABB has recently become more actively concerned about blood center administration; to date, the AABB has oriented itself primarily to hospital blood banks and to the day-to-day technological aspects of blood services.) CCBC describes itself as serving as a forum for blood center administrators, medical directors and senior management. It publishes no technical or procedures manuals, and does not operate

a formal resource exchange system, but holds two meetings a year to discuss management issues. CCBC is a relatively small organization which has struggled financially in the past. It derived almost all of its $207,000 income in 1983 from membership dues (136).

Each of the three organizations described above also serves its members or chapters by representing them on the American Blood Commission's Board of Directors.

American Blood Commission (ABC)

The American Blood Commission is the one formal mechanism enabling the AABB, ARC, and CCBC to work together, along with other health care providers (e.g., American Hospital Association, American Medical Association), consumer groups (e.g., National Hemophilia Foundation, National Kidney Foundation, American Legion), and representatives from the commercial plasmapheresis industry (e.g., Pharmaceutical Manufacturers Association of America). A list of ABC's members and governing board is shown in table 12.

Given its unique position as a private voluntary association charged with implementing public policy, ABC has been forced to influence blood policy through nonregulatory channels. Its potential effectiveness was limited by its lack of enforcement powers. In addition, philosophical differences persist among ABC's member blood collecting organizations, both voluntary and commercial, and the organizations fear losing control over their operations to the ABC. Many early attempts by the commission to mediate a compromise between the major blood collection organizations failed. For example, while ABC's Board adopted the recommendation of its 1977 Task Force on Donor Recruitment that the nonreplacement fee be abolished, it was never acted upon by the full commission because of AABB's opposition.

Some of ABC's programs and initiatives are widely credited for catalyzing change in the blood industry-or at the very least, for maintaining constructive dialog conducive to problem-solving. It has been suggested that ABC may have succeeded in its role as conscience of the blood industry (270) by providing a public forum for discussion of blood policy issues. ABC has established standing committees on donor recruitment, and regionalization, for example; both are issues in which the exchange of information, and an eventual consensus, are of value both to the industry and to those served by it.

ABC, and many others, see its regionalization recognition program as having been fairly successful, with 44 regions, representing over 50 percent of the Nation's blood supply, having achieved full recognition status. ABC's attempt at a more far-reaching effort at resource sharing (which would have overcome the discontinuities between the AABB Clearinghouse and the ARC system) was delayed when the commercial sector objected to limiting resource sharing to noncommercial blood, and the Red Cross withdrew in fear that a civil suit would be filed. The Red Cross has substantial assets which it fears could be attached if such a suit were filed and won.

In an attempt to get an agreement about resource sharing signed, the ABC Board contemplated, but never enacted, a motion to seek Federal legislation that would, in effect, exempt participation in resource sharing from antitrust action. The strategy now is to see whether the move of the AABB National Clearinghouse operation to the Washington, DC, area will make resource sharing seem more feasible. The continuing failure of the blood collectors to agree on a means of coordination has been frustrating to the consumer representatives on the ABC Board, but it is not clear that such coordination would contribute significantly to the efficiency of blood collection (see ch. 5, pt. 2).

ABC's effort at coordinating an ongoing system of data collection and analysis was a mixed success. While the 1979 and 1980 data collected for the ABC's National Blood Data Center represent the only systematic national data collection since 1972, ABC was unable to maintain data collection on an ongoing basis, or to make it commercially viable, as had been hoped. The effort was marked initially by heated debates among the participating organizations (e.g., *on the collection* of information on outdated blood, which was defined differently by different organizations (270; see also 547). Further, National Blood Data Center data do not include information on the com-

Table 12.-American Blood Commission Member Organizations and Its Board of Directors, April 1984

Member organizations:
American Association of Blood Banks
American Association for Clinical Histocompatibility Testing
American Association of Donor Recruitment Professionals
American Association of Retired Persons
American Association of Tissue Banks
American College of Physicians
American College of Surgeons
American Federation of Labor—Congress of Industrial Organizations
American Heart Association
American Hospital Association
American Legion
American Medical Association
American Nurses' Association, Inc.
American Osteopathic Association
American Red Cross
American Society of Anesthesiologists
American Society for Apheresis
American Society of Clinical Pathologists
American Surgical Association
College of American Pathologists
Communications Workers of America
Cooley's Anemia Foundation
Council of Community Blood Centers
Health Insurance Association of America
Leukemia Society of America
National Association for Sickle Cell Disease, Inc.
National Association of Patients on Hemodialysis and Transplantation, Inc.
The National Hemophilia Foundation
Pharmaceutical Manufacturers Association
United Way of America
Veterans Administration

Board of Directors:
Ray Andrus
American Federation of Labor—Congress of Industrial Organizations
J. Newton Ashworth, Ph.D.
Pharmaceutical Manufacturers Association
Fred A. Barnette, at-large
Ortho Diagnostics, Inc.
Carl G. Becker, M.D.
American Heart Association
Hamp Coley
United Way of America
Margaret M. Diener, MPH
National Association of Patients on Hemodialysis and Transplantation, Inc.
Suellyn Ellerbe, R. N., M.N.
American Nurses' Association, Inc.
Ralph G. Golden, Ph.D.
American Association of Retired Persons
Charles R. Goulet
Blue Cross/Blue Shield Association
David Guri, at-large
Alpha Therapeutic Corp.
Douglas Holloway, at-large
James B. Hubbard, Vice President
American Legion
Alfred J. Katz, M.D.
American Red Cross
Roland H. Lange
American Red Cross
Paul McCurdy, M.D.
American Society of Hematology
Franklin D. McDonald, M. D., Secretary
National Kidney Foundation
Mary L. Mays
Communications Workers of America
Harold T. Meryman, M.D.
American Association of Tissue Banks
John D. Milam, M.D.
American Association of Blood Banks
William V. Miller, M. D., President, at-large
Gerald S. Moss, M. D., FACS
American College of Surgeons
Victor H. Muller, M.D.
American Society of Clinical Pathologists
Richard E. Palmer, M.D.
American Medical Association
Peter J. Quesenberry, M.D.
Leukemia Society of America
Randall H. Rolfe
American Hospital Association
Dale A. Smith, at-large
Baxter-Travenol Laboratories, Inc.
James M. Stengle, M.D.
The National Hemophilia Foundation
Bill T. Teague, B. S., M.T. (A. S. C.P.), S.B.B., Treasurer
American Association of Blood Banks
John L. Thornton, M. D., Vice President
Council of Community Blood Centers
Martin J. Valaske, M.D.
College of American Pathologists
Edward L. Wampold, at-large
Cooper Diagnostics
Charles F. Whitten, M.D.
National Association for Sickle Cell Disease, Inc.
Edward C. Zaino, M.D.
Cooley's Anemia Foundation

SOURCE: American Blood Commission.

mercial plasmapheresis industry, which was collected and published separately by the American Blood Resources Association.

Government support for ABC has diminished over the years, necessitating increases from private funding (see table 13). ABC now receives no Federal funding. A great blow was the withdrawal of the American Cancer Society, the American College of Emergency Physicians, the American Osteopathic College of Pathologists, and the National Medical Association in **1983.** Although members are often delinquent in their dues, collections of membership dues for fiscal year 1984

Table 13.—American Blood Commission Statements of Support, Revenue, and Expenses and Changes in Fund Balances for Years Ended Mar. 31, 1976-83 (thousands of dollars)

	1983	1982	1981	1980	1979	1978	1977	1976
Public support:								
U.S. Government contracts	$56	$296	$467	$337	$348	$526	$389	$129
Private grants					12	42		100
Contributions	126	123	46	51	61	46	7	
Total public support	$182	$419	$513	$389	$420	$614	$395	$229
Revenue:								
Membership dues	$166	$169	$179	$179	$159	$144	$144	$141
Investment income	20	19	9	8	3		1	4
Conference fees	10	8	23	10				
Publications and miscellaneous		22	6	3	2	2		
Loss on sale of equipment	(3)							
Total revenue	$202	$219	$217	$200	$163	$147	$144	$145
Total support and revenue	$384	$638	$730	$589	$583	$761	$540	$374
Expenses:								
Program services:								
Technical advisory panel	*3*	*3*	*16*					
Resource sharing		12	8					
Policy operations	93	137	142	173	149	139	169	
National Blood Data Center	73	240	277	191	165	237	106	29
Regionalization	57	84	103	70	87	88	72	36
Management and Logistics Conference			8	3				
Plasma study			2	4				
Utilization					5	7	4	
Long range planning					1			
Commonality						46	107	39
Clearinghouse						5	5	
Donor recruitment						44	63	20
Planning and implementation								35
Total program service expenses	$225	$475	$555	$440	$407	$565	$525	$158
Supporting services:								
Management and general	$110	$157	$178	$141	$119	$172	$ 85	$40
Financial development	7	4	13	2	21			
Total supporting services	$117	$161	$190	$143	$139	$172	$85	$40
Total expenses	*$342*	*$636*	*$746*	*$583*	*$547*	*$737*	*$609*	$199
Excess (deficiency) of public support and revenue over expenses	$42	$ 2	$(16)	$ 6	$37	$24	$ (69)	$175
Fund balances, beginning of year	157	156	172	166	129	106	175	
Fund balances. end of year	$199	$157	$156	$172	$166	$129	$106	$175

SOURCE American Blood Commission, 1983

exceeded ABC's goal. Nevertheless, as a consequence of corporate contributions not meeting ABC's goal, ABC now projects a $20,000 shortfall in fiscal year 1985. Some believe that the decline in support indicates that there is no longer a need for such an organization to resolve differences among blood collectors.

Blood Collections in the Voluntary Sector

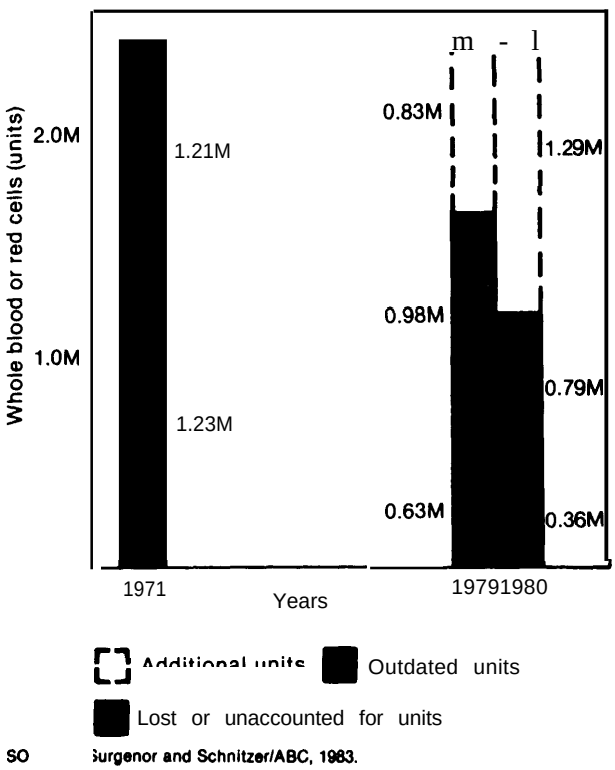
Whole blood collections have been able to keep up with increasing demand at the same time that paid whole blood donations have decreased significantly (fig. 1 in ch. 1). This increase has occurred through increased recruitment, improved inventory management, and a large increase in the use of blood components instead of whole blood.

The most recent comprehensive data on whole blood collections and transfusions are for 1979 and 1980 (518). Partial data are available from blood collection centers (but not transfusion services) represented by ARC, AABB, and CCBC for 1981 (29) and from the American Red Cross through June 1983. In 1980, out of 11.15 million units of whole blood collected, 14.8 million units of blood components were transfused, exclusive

of blood that was outdated or lost (see fig. 2 in ch. 1). Between 1971 and 1980, whole blood collections increased from 8.8 million to 11.15 million units, 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 (see fig. 5). (Solutions increasing the storage life of blood from 21 to 35 days were introduced in 1980, and this effect is only partially reflected in the 1980 data. Recent approval of a solution that allows a 49-day shelf life for packed red cells should result in further improvement, although the additional cost of such solutions may limit their widespread acceptance.)

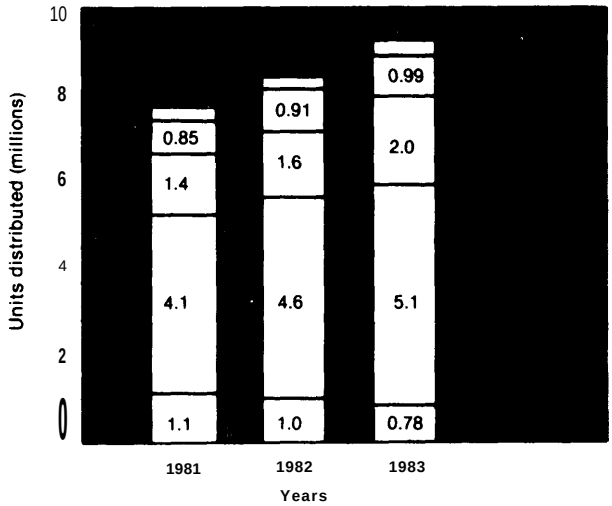
Losses in Red Cross centers have remained fairly stable in the years since 1980 but these data do not include reports from hospitals and other blood banks to which blood is shipped. Red Cross data shown in figure 6 for products distributed for transfusion (but not necessarily transfused) indicate that trends toward component therapy and the use of blood components have continued.

Figure 5.—Increases in Red Cells Available for Transfusion As a Result of Improved Inventory Management and Decreased Outdating



SOURCE: Surgenor and Schnitzer/ABC, 1983.

Figure 6.—Recent Trends in Whole Blood and Components Distributed for Transfusion
(Red Cross data only)



SOURCE: American Red Cross, *Blood Services Operations Reports: 1981-1983.*

Red blood cells (including whole blood) continue to dominate use and are the driving force behind collection efforts in the voluntary sector. Platelet use rose from 0.41 million units in 1971 to 2.86 million units in 1980. (Approval in 1982 of platelet storage bags that extend the storage period from 3 to 5 days is expected to increase the availability and use of platelets, as well as to decrease outdating, which is substantial.) Most platelet concentrates are made from whole blood, but platelets are also collected directly (plateletpheresis). Plateletpheresis collections have increased steadily in Red Cross regions since 1979 (45,46,47,48). The reported nationwide drop in plateletpheresis collections between 1979 and 1980 (518) may be misleading because of a simultaneous increase in combined leukaplateletpheresis procedures (470).

Fresh-frozen plasma (FFP) production has also increased, although indications for its use are limited and have become the topic of private and Federal scrutiny (see ch 5, pt. 4). In the Red Cross alone, 3.2 million units of FFP were produced in 1983, a 27.2-percent increase over the previous year. However, only 30 percent of the fresh-frozen plasma produced was distributed for transfusions. Two-thirds was used for fractionation.

Use of the final product from voluntary whole blood collections, cryoprecipitate, which contains antihemophilic factor (AHF) and other coagulation proteins, remained constant from 1972 to 1980, primarily because of availability of a more effective and stable way to inject concentrates of AHF derived from pooled plasma. However, in light of the AIDS crisis, and because new uses have been found for the substance (see ch. 5, pt. 4), cryoprecipitate production has increased recently (23,48).

Costs of Blood and Blood Components

On the whole, the cost of blood and blood products has not been a major factor in discussions of health care expenditures, probably because it has been estimated that the total valuation of collected and transfused blood and blood products (including plasma derivatives) is only about 1 percent of total health care expenditures (31a). However, the National Blood Policy (NBP) pointed out that costs could have an impact on access to health care. Another issue addressed by the NBP was the need for public confidence in the reasonableness of service charges to encourage voluntary donors. To this end, the National Blood Policy encouraged development of accounting and reporting systems to identify relationships between the costs and charges for all services and materials associated with transfusion therapy (180; see table 2 in ch. 2).

In 1979, the U.S. General Accounting Office recommended that the Health Care Financing Administration (HCFA) investigate the relationship between costs and charges for blood products to determine if Medicare was being overcharged by hospitals (546). Concern had also been raised about whether nonreplacement fees constituted "profiteering," especially when patients were charged for nonreplaced blood that was originally obtained from unremunerated donors (e.g., see 511). The nonreplacement fee was also viewed as causing problems of access to health care for Medicare patients, who are responsible for paying a three-unit deductible if they cannot arrange to replace the blood transfused in hospitals charging a nonreplacement fee.

Costs and Charges for Blood Products

The costs associated with voluntarily donated blood derive from donor recruitment, equipment (hardware and software) and labor, testing, inventory management and distribution, and transfusion. When donors are paid, the costs of remuneration must be added. Blood collecting and transfusing facilities in the voluntary sector have not developed a uniform industrywide system for allocating costs to each step in the collecting and transfusing process. The American Red Cross and some larger independent blood centers (e.g., the New York Blood Center) have developed cost accounting systems for internal use.

There is wide variation in the fees charged to hospitals and patients by blood collectors and by hospitals to patients. As shown in table **14, 1983** processing fees for whole blood charged by American Red Cross regions ranged from **$28** (in San Juan, PR) to $59 (in San Jose, CA). Charges in some community blood centers can be higher, e.g., **$67** for whole blood in San Mateo, CA (including a replacement fee); $75 at the Irwin Memorial Blood Bank in San Francisco. Similar variations are found for other components. Production and sale of the several blood components means that an average Red Cross blood center could collect up to $105.54 from a single unit of whole blood donated in 1983, not including revenues from recovered plasma (higher if red cells are frozen or washed).

Increases in processing fees for blood components, as well as better inventory management, have meant that blood suppliers have been able to accumulate substantial fund balances. For example, as shown in table 15, Red Cross net assets at year-end increased by 18 percent from 1980 to 1981, by 30 percent from 1981 to 1982 and by 32 percent from 1982 to 1983. Although apparently substantial on a cumulative basis, Red Cross net assets of $36,053,000 for the year ended June 30, 1983, amounted to only 8.5 percent of that year's entire blood services revenues, representing fewer than 36 days of operating expenses, according to the Red Cross (43). Some blood centers (e.g., Puget Sound Blood Center, Hoxworth Blood Center) have deliberately accumulated revenues over

Table 14.–Blood Center Processing Fees for Blood and Components (1983)

Blood components	Average processing fees ARC	CCBC	Range[a]
Whole blood	$ 41.83	$42.59	$28.00 (San Juan)–$ 59.00 (San Jose)
Red blood cells	41.17	40.41	28.00 (San Juan)— 59.00 (San Jose)
Red blood cells deglycerolized	131.55	—	91.00 (Portland) – 225.00 (Atlanta)
Red blood ceils washed	86.00	NA	60.25 (Roanoke) — 160.00 (Atlanta)
Fresh-frozen plasma	25.08	24.49	17.00 (Waco) – 38.00 (San Jose)
Cryoprecipitated AHF	12.28	12.68	8.00 (Great Falls, Daytona) — 18.00 (4 centers)
Platelets	26.41	25.31	17.00 (Waco) — 40,00 (Boston)

[a]Red Cross data only.
NA = not available.

SOURCES ARC—American Red Cross (1983), fees shown are as of June 30, 1983, and do not include the **NYBC; CCBC—Huitt, letter to OTA, 1964; fees shown are as** of July 1983.

those required for operating expenses in order to provide for capital expansion (221,242). Red Cross headquarters usually does not exercise direct control over blood services assets; such assets are used at the discretion of individual blood services regions (141). A small portion of Red Cross revenues is devoted to research—less than 2 percent.

The difference between community blood center processing costs and hospitals' charges to patients is shown in table **16.** In table 17, the processing fee for red cells charged by blood centers to hospitals is compared to hospital charges to patients. In 1980 the average community blood center red cell processing fee to hospitals was about $32. (The average cost of $45.91 for collecting and processing a unit of whole blood is offset by sales of remaining blood components.) The average total hospital charge for a unit of red cells was $88.97. In addition to a processing fee, hospital charges might include an additional processing fee, a replacement charge, a laboratory charge, an infusion charge and other charges (table **16).** Data for processing fees for hospitals include hospitals which also collect their own blood. Wallace & Wallace/ABC (576) found that total charges are higher at collecting than at noncollecting hospitals, and that higher processing fees and replacement fees accounted for the higher total charges. As might be expected, there is substantial variation 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.

Increases in blood costs have not exceeded increases in total health care costs. As shown in table 17, national health expenditures have increased on an average of 15 percent per year (for 1980 to 1982), while blood center processing fees have increased 7 percent (CCBC members) and 12 percent (Red Cross regions). Increases in hospital charges for blood appear closer to increased hospital charges in general, although it is difficult to draw conclusions with information from only 2 consecutive years.

Access

Issues of access are more difficult to sort out than issues of cost/charge relationships. It is currently unlikely that individuals will be denied hospital care because they cannot afford the cost of blood to be transfused during their hospital stay, but the issue may become more complicated as prospective payment systems are phased in (see ch. 5, pt. 4). At present the only real threat to access posed by the cost of blood products seems to be that uninsured hemophiliacs may receive less Factor VIII than is optimal.

At present, there is wide variation in the way third-party payers cover the costs of blood products. Since 1968, Blue Cross/Blue Shield national policy has been to encourage voluntary donation and replacement, and blood assurance programs (79). Like Medicare, then, most Blue Cross/Blue Shield policies have a three-unit deductible for nonreplacement fees when they are charged. For Federal employees covered by Blue Cross/Blue Shield, however, replacement fees are partially covered by the supplemental portion of the policy (i.e., 80 percent coverage for high option; 75 percent coverage for low option). Policies more costly to patients are followed in at least one State.

Table 15.—American Red Cross Blood Services Statements of Revenue and Expenses and Statement of Assets and Liabilities, 1980-83 (for the year ended June 30) (in thousands)

	1983	1982	1981	1980
Revenues:				
Blood Services processing	$418,962	$371,901	$301,685	$241,155
Investment income	5,389	3,695	2,252	1,213
Contributions	177	200		—
Government and private foundation grants	73	101	66	209
Other income	1,292	1,371	2,016	1,021
Total revenues	425,893	377,268	306,019	243,598
Expenses:				
Blood Services expenses	379,091	342,813	292,281	233,684
Less—expenses incurred by chapters funded from non-Blood Services support and revenue	(9,821)	(9,469)	(9,673)	(10,633)
Net Blood Services expenses	369,270	333,344	282,608	223,051
Excess of revenue over expenses before property and equipment acquisitions	56,623	43,924	23,411	20,547
Property and equipment acquisitions—net of proceeds from sales of property	(20,570)	(17,927)	(10,130)	(9,577)
Net Excess of Revenues Over Expenses and Property Acquisitions:				
Increase in designated balances approved by Board action for:				
Replace and improvement of buildings and equipment	9,271		—	—
Other specific purposes	6,193	.	—	—
Net operating assets required	20,589		—	—
	36,053	25,997	13,281	10,970
Designated Net Assets, Beginning of Year	111,364	85,367	72,086	61,116
Designated Net Assets, End of Year	$147,417	$111,364	$ 85,367	$ 72,086
Assets:				
Cash and time deposits ..,	$ 14,392	$ 6,425	$ 5,982	$ 6,658
Investments	46,415	29,350	15,181	9,365
Receivables	47,745	47,073	41,458	31,129
Inventories	55,116	47,268	51,975	52,351
Other assets...	1,084	799	541	353
Due from undesignated funds	8,172	4,015	—	—
Total assets	172,924	134,930	115,137	99,856
Liabilities:				
Accounts payable and accrued liabilities	25,480	23,132	20,018	15,136
Notes payable	27	434	494	602
Due to undesignated funds	—	—	9,258	12,032
Total liabilities	25,507	23,566	29,770	27,770
Net Assets	$147,417	$111,364	$85,367	$ 72,086
Net assets—as follows:				
Replacement and improvements of building and equipment	*$20,511*	$ 11,240	$ 6,577	$ –
Other specific purposes	*16,405*	—	—	—
Net assets required for operations	*110,501*	100,124	78,790	—
Net assets—as above,	$147,417	$111,364	$85,367	—
Notes: Compared to:				
● Total ARC Public Support and Revenue	$722,159	$637,059	$556,911	$484,300
● *Total Net Assets of ARC	628,658	559,949	231,298	214,647

SOURCE American Red Cross Annual Report, 1980-83.

Table 16.—Blood Center Costs and Hospital Charges for Red Cells, 1980

Average community blood center cost per unit whole blood collected . . .	$45.91 (15.34)[1]
Average total hospital charge for unit of red cells	88.97
Charges may include:[b]	
Processing fee (average)	37.94
Replacement fee (average)	27,54
Laboratory fee (average)	40.51
Infusion fee (average)	20.41
Other (e.g., blood delivery, general administration), ...	17.32

[a] Figure in parenthesis is standard deviation.

[b] Charges do not add to total average hospital charge because not all hospitals charge all types of fees. Of the 2,441 respondents to the survey conducted by Wallace and Wallace/ABC, 2,250 charged a laboratory fee, 1,756 charged a processing fee, 1,656 charged an infusion fee, 351 charged a replacement fee, and 60 charged a fee related to some other service.

SOURCE: Wallace and Wallace/ABC, 1982.

Mississippi Blue Cross/Blue Shield has a three-unit deductible for all costs associated with blood transfusions, including processing charges and administration charges.

Some blood centers offer coverage incentives to donors in addition to replacement credits. The Gulf Coast Regional Blood Center in Houston has two blood assurance plans. "Life Plan I," for families and individuals covers the donor (and certain selected others) for all Gulf Coast Regional Blood Center service fees for blood and blood components transfused in the gulf coast region served by the blood center. Hospital charges for typing and crosshatching etc. are not covered, and, as in most insurance plans, preexisting conditions are not covered. "Life Plan II" is a group plan which fully covers participating donors and their immediate families and also provides partial coverage (equal to one replacement donation) for nondonors in the group, if there is 25 percent participation. Gulf Coast also charges and covers replacement fees.

Mississippi Blood Services (MBS) has probably the most generous coverage plan for donors. Its "donor protection program" covers any out-of-pocket blood charges (including any hospital replacement fees) up to $10,000 for any MBS donor, without geographic restrictions. MBS itself does not charge a replacement deposit fee. In 1983, MBS paid out-of-pocket blood charges amounting to $51,163 for 393 patients. The largest single payment for one patient was $3,759. MBS acknowledges that such a system would not be feasible for blood centers on a large-scale basis because insurance companies might increase their deductibles if such a plan were adopted nationwide, or even in entire regions.

Table 17.—Changes in Processing Fees for Red Cells Compared to Changes in Total U.S. Health Care Expenditures

Processing fees charged by community blood centers	ARC	CCBC[3]	Percent change from previous year ARC	Percent change from previous year CCBC	Percent change in national health expenditures[4]
1976-77	22.19[1]	n/a	—	—	11.9
1979	n/a	32.30			13.5
1980	30.23[2]	34.14	*8.04*	5.7	15.8
1981	38.30[2]	36.98	*26.7*	7.7	15.1
1982	38.80[2]	39.72	*1.3*	7.4	12.5
1963	41.47[1]	40.41	*6.9*	1.7	n/a

Hospital charges[5]	Total	Processing Fee	Replacement	Laboratory	Infusion	Other
1979	79.06	32.07	28.31	33.94	19.94	13.60
1980	88.97	37.94	27.54	40.51	20.41	17.32
Percent change 1979-80	13%	18%	–3%	19%0	20/0	270/o

n/a = not available.

SOURCES: [1]Wallace and Wallace/ABC, 1982.
[2]American Red Cross Operations Reports; data as of June 30.
[3]Huitt, personal communication, 1984; data for 1983 is as of July.
[4]Gibson, R. M., Waldo, D. R. and Levit, K. R., *National Health Expenditures, 1982*.
[5]Wallace and Wallace/ABC, 1982.

PART 2: THE COMMERCIAL PLASMA AND PLASMA DERIVATIVES SECTOR

Overview

Demand for large amounts of plasma, principally for production of albumin, antihemophilic factor (AHF, or Factor VIII), and immune serum globulins, has led to what is known as the "source plasma" industry, in which donors provide plasma, not whole blood.

The source plasma sector is largely commercial and has three main components: collectors, or plasmapheresis centers; fractionators; and brokers, all of whom operate on a for-profit basis. Not-for-profit blood banks and blood centers also play a part in the commercial plasma industry when they sell recovered or salvaged plasma (i.e., plasma recovered after components have been removed from whole blood, or after whole blood has outdated) to fractionators, or when they contract with commercial firms to fractionate plasma into derivatives which they then market themselves.

Forty-five percent of the Red Cross' recovered plasma is fractionated by commercial fractionation companies (486). It is estimated that from 17 to 20 percent of the plasma derivatives sold in the United States is sold by the voluntary sector (i.e., by the Red Cross and the New York Blood Center). These sales put the not-for-profit industry in direct competition with the commercial plasmapheresis industry.

As shown in table 18, at present there are approximately 336 source plasma centers licensed by the FDA: 317 U.S. centers are commercially operated, and 19 are community or Red Cross blood centers—i.e., they are not operated for profit. The largest portion (90 percent) of source plasma centers is owned by independently operated multi-location companies. These multi-location centers are owned by 30 companies marketing biological products. Some of these biological companies are subsidiaries of larger corporations (e.g., Sera-Tec Biological, owned by the Rite-Aid Corp. in New York, operates nine centers in the East and Midwest, most of which are near college campuses). The plasma collected by commercial plasmapheresis centers is either sold to U.S. fractionators who separate it into a number of products, primarily 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 companies "self-source"; i.e., they run their own source plasma centers. According to the latest figures, 98 (30 percent) of the U.S. source plasma centers are owned by fractionation companies. Most centers contract annually with fractionators to provide a certain amount of plasma, although there is some "spot buying. " Recovered plasma (from whole blood) is not contracted for, but is 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 (437).

Table 18.-Number of Plasma Centers Located in the United States
(by owner, fractionator, multi-operator, single operator, and nonprofit)

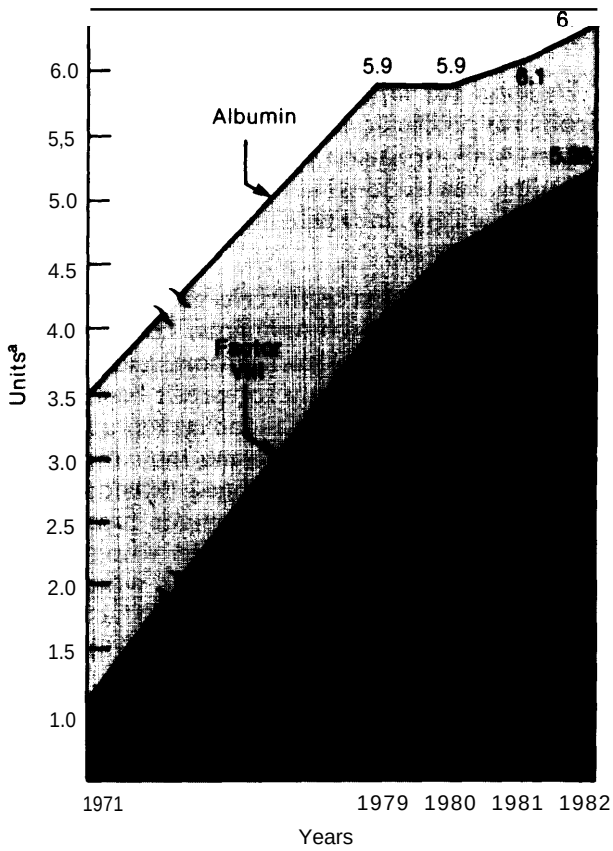
	Nov. 1979	July 1980	Mar. 1981	Apr. 1984	Percent change
Fractionator owned	121	123	107	92	– 24%
Multi-operator	171	167	213	177	+ 4%
Single operator	98	104	50	48	– 51%
Non-profit	9	9	11	19	+ 110YO
Total	399	403	381	336	– 160/0

SOURCE: Plasma *Ouarterly,* summer 1984,

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 of plasma fractionated in the United States annually (459). In addition, the nonprofit New York Blood Center operates its own 300,000-liter-capacity plant for fractionating plasma recovered from its own donors and from a portion of Red Cross donors. (The States of Michigan and Massachusetts each have small [approximately 50,000 liters each] fractionation capacities, with derivatives distributed primarily in each State.)

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 in chapter 1. About 1.3 million of the 6 million liters of source plasma are exported, in addition to the exportation of plasma derivatives manufactured in the United States. About 5.5 million of the 12.5-million-liter worldwide manufacturing **capacity** in 1978 was in the United States. Of the 7-million-liter capacity outside the United States, about 5 million liters were in the commercial sector, and about 2 million liters were in the voluntary sector. But there were only about 77 plasma fractionation firms worldwide (439), and commercial plants outside the United States operate at about 68 percent capacity, compared to about 85 to 90 percent of capacity in the United States (459). As shown in figure 7, domestic production of AHF and albumin have increased steadily. In 1971, 110 million activity units of Factor VIII were sold; in 1982 the figure **was** 528 million. Comparable increases have occurred for albumin. Albumin accounts for the largest share of total sales (see table 1 in ch. 1). It is estimated that in 1984, approximately one-third of the albumin and one-half of the Factor VIII produced will be used in foreign countries (see table 19).

Figure 7.—U.S. Production of Factor VIII (in activity units) and of Albumin/PPF (in 12.5 Gram Equivalents), 1971-82



[a]Albumin/PPF in millions of 12.5 gram equivalents; Factor VIII in hundreds of millions of activity units.

SOURCE: Rodell, personal communication, 1983.

Thus, much of the plasma and plasma derivatives used worldwide comes from U.S. sources.

The principal products of the source plasma industry that are used in this country are albumin, AHF, and plasma protein fraction (PPF), which is used much as is albumin. Other products include intravenous gamma globulin (IVGG), immune serum globulin and hyperimmune globulins. Worldwide use differs from use in the United States. For example, in 1978, at a time when IVGG was not licensed in the United States, it accounted for 23 percent of worldwide demand for

Table 19.—Production and Consumption of Human Serum Albumin and Antihemophilic Factor

	1971	1976	1979	Forecast 1984
Plasma processed in the United States (thousands of liters)	1,950	2,910	3,950	6,920
HSA production in the United States (millions of grams)	39	67	91	159
HSA consumption:				
Domestic (millions of units)	2.9	4.6	5.8	8.5
Foreign (millions of units)	0.3	0.7	1.5	4.2
Total (millions of units)	3.2	5.3	7.3	12.7
Domestic	940/0	870/o	800/0	670/o
Foreign	60/0	13 "/0	20 "/0	330/0
HSA revenues:				
Domestic (millions of dollars)	$58	$133.4	$168.2	$300
Foreign (millions of dollars)	4	20.3	43.5	148
Total (millions of dollars)	62	153.7	211.7	448
Plasma processed globally for AHF (thousands of liters)	365	1,600	2,750	5,320
AHF units processed (millions)	80	400	688	1,330
Domestic consumption:				
Millions of units	72	300	412	648
Average price (cents/units)	15	10	10	14
Sales (millions of dollars)	10.8	30	41.2	91
Foreign consumption:				
Millions of units	8	100	275	682
Average price (cents/units)	40	30	30	27
Sales (millions of dollars)	3.2	30	82.5	184
Total AHF sales (millions of dollars	14	60	123.9	275

SOURCE: Office of Technology Assessment, based on data and estimates in M M. Le Coney, "Who Needs Plasma?" Plasma Ouarterly 2:68-93, September 1980.

plasma fractions (see table 1). Table 20 summarizes differences in albumin/PPF consumption between selected countries in 1976.

Sources of Raw Plasma

In the 1960s, the introduction of plastic bags for collection of whole blood enabled component separation to increase, and blood centers began to address the need to more effectively utilize plasma from whole blood. Today, plasma in excess of a region's needs is supplied by blood centers to plasma derivative manufacturers for further processing. Plasma is supplied as fresh-frozen plasma or liquid recovered plasma to licensed processors (253).

Table 20.—Albumin and Plasma Protein Fraction Consumption unselected Countries, 1976

Country	Consumption in kilograms 1 million population
West Germany	499kg
United States	301
Austria	259
Finland	213
France	59
Japan	50
Brazil	14

SOURCE" Adapted fromT. Drees, Plasma Forum, 1979,

The American Red Cross, which has been involved in providing plasma for fractionation since the pioneering work of E. J. Cohn, does not operate any facilities for production of plasma derivatives. One regional blood center, the New York Blood Center (NYBC), has its own plasma fractionation facility. The Red Cross maintains a number of contracts with domestic and foreign plasma fractionation facilities to process Red Cross plasma in accordance with Red Cross specifications, and the products are returned to Red Cross regional blood centers for distribution to hospitals and other users (319). Through its system of regional blood centers, the Red Cross collects more plasma for fractionation than any other single entity in the world. As described earlier, however, the vast majority of the plasma required to meet the needs of the United States and other parts of the world is provided by commercial plasmapheresis centers. While some of the major manufacturers operate their own plasma collection centers, many are operated by independent multi-location companies.

Plasmapheresis has several advantages over recovery of plasma from a single unit of whole blood, First, the volume of plasma recovered per donation is greater with plasmapheresis. Up to 600

ml of plasma can be taken per donation, versus an average recovery of 200 to 250 ml per donation of whole blood. Second, under current FDA guidelines, a donor can be plasmapheresed twice each 7 days, while a whole-blood donor can contribute only once every 8 weeks and a maximum of five times per year. Third, because plasmapheresis collections are specifically for fractionation into derivatives, the plasma is frozen immediately upon collection, thereby preserving more of the labile protein fractions whose functional loss is proportional to delays in freezing.

Finished plasma derivatives for the U.S. market are produced and supplied by several companies. Most manufacturing facilities that produce human plasma derivatives are located in the United States, but some are located in Europe and Canada. The principal producers of human plasma derivatives for the U.S. market are identified in table 21. None of these licensed manufacturers produce all of the plasma derivatives approved for distribution in the United States. In addition to those listed, numerous other manufacturers produce plasma derivatives for use in other parts of the world (319).

The cost of plasma is generally determined by the number of products that can be made from the plasma and the anticipated protein yield. Frozen source plasma, collected by plasmapheresis, and fresh-frozen plasma obtained from whole blood but frozen shortly after processing, have traditionally provided the highest product and protein yield. Although all plasma processing is based on the basic Cohn process (described in ch. 4), modifications and improvements in methods or equipment enable some fractionators to process plasma more cost effectively than do their competitors.

The time from collection to processing into licensed, finished products takes as much as 4 to 6 months, depending on the products produced and the manufacturer. Temporary shortages and surpluses can occur, with parallel increases and decreases in price. In addition, such factors as price variances between nations, due to prices governments and insurance plans pay for a particular plasma derivative, affect where products are distributed. Many manufacturers have distribution networks in numerous countries and direct their products to the markets where demand is great and prices are higher.

Barriers to entry into the plasma fractionation business are substantial, due to the need to develop cost-effective production techniques, construction of a capital-intensive facility, and stringent licensing requirements for biological products. For these reasons and the volatile and competitive nature of the plasma derivatives market, no new production facilities have been constructed in the past 12 years by firms not already in the business. In the recent past, except for continued marketing of some immune globulins, several firms have left the plasma derivatives market, including large pharmaceutical firms such as Parke-Davis, Squibb, Upjohn, and Merck Sharp & Dohme.

Table 21.—Principal Producers of Human Plasma Derivatives for the U.S. Market

Company	Manufacturing location	Ownership
Alpha Therapeutics	California	Green Cross/Japan
Armour	Illinois	Revlon/USA
Connaught	Canada	Connaught/Canada
Cutter	North Carolina	Bayer/Germany
Hyland	California	Baxter Travenol/USA
Immuno	Michigan/Austria	Immuno/Austria
Massachusetts State Laboratory	Massachusetts	State of Massachusetts
Michigan State Laboratory	Michigan	State of Michigan
New York Blood Center	New York	New York Blood Center
Swiss Red Cross	Switzerland	Swiss Red Cross
Netherlands Red Cross	Netherlands	Netherlands Red Cross

SOURCE: Grossman & Schmitt, 1984

Finished Products Licensed for Use in the United States

Normal Serum Albumin and Plasma Protein Fraction

Normal serum albumin (NSA) and its close relative, plasma protein fraction (PPF), are produced from Cohn Fraction V, with PPF also containing proteins from Cohn Fraction IV-4. Under FDA standards, greater than **96** percent of the protein in NSA must be albumin, while for PPF the requirement is that only greater than 85 percent of the protein in the solution must be albumin. The production of PPF instead of NSA is economically advantageous to plasma fractionators due to the allowed differential in albumin concentration in the final product.

Normal ***serum*** albumin is available in 5 and 25 percent concentrations in various vial sizes. PPF is available ins percent concentrations in various vial sizes. NSA and PPF are generally regarded as generic products by users, and distributors and hospitals often obtain these products from several sources (319).

Many of the major manufacturers of NSA and PPF often contract to deliver their products to users on a direct basis. The need for these products and the size of the market requires that numerous outlets be made available. Users include hospitals, nursing homes, dialysis centers and pheresis centers, as well as the local physician who requires an occasional vial to treat a patient in his office.

NSA and PPF account for approximately one-half of the total dollar volumes of plasma derivatives distributed in the United States. In the last 5 years, there has been a steady decrease in the use of PPF, with increasing use of 5 percent NSA displacing PPF (486).

One liter of plasma processed into NSA will yield approximately 25 grams of protein. Based on market prices in mid-1984, the value of the product would be between $2.50 and $2.80 per gram, or between $62.50 and $70.00 per liter of plasma. The manufacturers that operate FDA-licensed facilities for the processing of plasma into NSA and PPF for the U.S. market are listed in table 22.

Table 22.—Manufacturers of Normal Serum Albumin (NSA) and Plasma Protein Fraction (PPF) Licensed for Use in the United States

Alpha Therapeutics
Armour Pharmaceutical
Connaught Laboratories
Cutter Biological
Hyland Laboratories
Immuno
Massachusetts State Laboratory
Michigan State Laboratory
New York Blood Center
Netherlands Red Cross
Swiss Red Cross

SOURCE: Grossman & Schmitt, 1984

Although there are numerous distribution outlets, the vast majority of these products are supplied by the manufacturers and the Red Cross directly to hospitals. Distributors are used to service the specialized needs and regional requirements of other users.

Every institution that uses NSA and PPF independently determines the purchasing method that provides it the most benefits. The various purchasing alternatives currently available are: 1) arranging an independent purchase contract with a manufacturer, 2) participating in group purchasing contracts, 3) purchasing from local American Red Cross centers, and 4) purchasing from a community blood center or distributor. Institutions that have special requirements, in addition to negotiating prices, make these needs known to their suppliers. Some of these special requirements often preclude delivery of products in large shipments to one central warehouse facility. When this occurs, the cost of servicing an account is greatly increased, and manufacturers may lose the contract to smaller distributors or regional blood centers.

One of the most common ways of pricing NSA and PPF is by annual bidding from the various manufacturers and suppliers. Some hospitals negotiate annual prices with a local blood center or distributor that can provide supplies in quantities that meet the hospital's special needs.

Many not-for-profit hospitals have joined together to form joint purchasing groups. The concept of a joint purchasing program is that a supplier will bid a lower price if it can more easily obtain a substantial and reliable quantity of busi-

ness. Member hospitals provide the joint purchasing programs with projected use figures. The information is consolidated, and bids are solicited from approved manufacturers and suppliers.

Most purchasing groups operate as clearinghouses for information between their respective members and potential vendors, and never actually take delivery of the products. Orders are placed by each member institution directly with the supplier. Delivery and supply arrangements are coordinated between the hospital and the supplier. The purchasing group receives a rebate directly from the supplier, based on the actual volume of business, and manufacturers supply monthly reports to the purchasing groups.

Some purchasing groups or shared service corporations actually take ownership of the products. These purchasing groups provide warehousing and delivery services for its members as required. Shared service warehouses offer the hospitals numerous advantages, such as ordering all supplies, not only PPF and NSA, from one source. The manufacturer benefits by reducing costs for shipping and billing, since an order will only have to be sent to one location and billed to one account.

One of the problems arising from purchasing group programs is that manufacturers or distributors who are awarded supply contracts are required to rebate a specified percentage of the revenue to the purchasing group to offset its costs. Since these costs are paid by the supplier, they must be factored into the bid price and are ultimately paid by the hospital. The issue is often debated as to whether or not direct purchases could be made for less, especially by the larger hospital members.

The large chains of proprietary hospitals also solicit annual bids from the major producers. In many cases each hospital is given the opportunity to negotiate a more favorable supply arrangement with a local supplier. If a more favorable pricing arrangement cannot be made, the hospital can purchase from the vendor who has been awarded the national supply agreement for the chain. Dialysis centers and nursing homes requiring NSA and PPF usually negotiate with local sources at spot market prices because their requirements are often very sporadic.

In all cases, however, supply is a major factor. Reliability is often more important than saving a few cents per vial. When an organization can avoid having to carry a large dollar item in inventory, such as NSA and PPF, it often offsets these costs by purchasing from local sources rather than purchasing in large quantities from one of the manufacturers.

Supply and availability of all plasma derivatives are dependent on both the availability of the raw material (human plasma) and the prices obtainable for manufactured products. Prices as well as supplies have traditionally had very large "peaks and valleys." To offset price volatility, suppliers and manufacturers often resort to product transfer from one country to another.

Competition for business among the manufacturers and suppliers of NSA and PPF is very fierce. Traditional emphasis has been for pricing to act as the main element for differentiation. Purchasing groups which control a substantial volume of the NSA and PPF market tend to treat these products as commodities. The market is sensitive to price changes and thus maintains a high level of price-competitiveness. Margins earned by manufacturers on the sale of NSA and PPF are substantially below those characteristically earned on the sale of pharmaceutical products.

The second major determinant of consumer preference in the purchase of NSA and PPF is confidence in the suppliers's ability to fulfill its purchase obligation. Long production lead time, as well as sudden pricing shifts, make it difficult for suppliers to plan for and rapidly provide additional material. Some hospitals have encountered supply problems with a particular vendor and are often reluctant to purchase from that firm again, even if the price offered is lower than that of a competitor.

Other less significant determinants of purchaser preference are items such as packaging, which does affect sales to some accounts. Package size, type of intravenous hanger, cap or stopper, as well as the administration set used, have become competitive opportunities.

Differentiations between NSA and PPF products have become more related to the source of

service, packaging, and availability than to the product itself.

Coagulation Factors

Approximately one-quarter of the total dollar volume of plasma derivatives distributed in the United States are represented by coagulation factors, which are used for treatment of individuals with congenital deficiencies of Factor VIII or Factor IX. Antihemophilic factor, or concentrates of Factor VIII, is distributed and prescribed by the number of "activity units" desired. An "activity unit" is defined as that amount of Factor VIII present in 1 ml of normal plasma. The protein is very unstable and is therefore prepared as a lyophilized powder, which is reconstituted with sterile water prior to injection, AHF is available in reconstituted volumes of 10 to 40 ml, with associated activity unit ranges from **250 or 400 to 1,250 or 1,500.** Manufacturers licensed by the FDA for Factor VIII and Factor IX sales in the United States are listed in table 23.

All major plasma fractionators in the United States produce AHF (see table 23). Unlike other plasma derivatives, coagulation factors are produced only from plasma frozen within **24** hours of collection. The activity of these factors decreases rapidly unless the plasma is frozen and stored at —18 o C or colder until used by a plasma fractionator. Economics dictate that plasma be frozen as quickly as possible after collection in order to maximize product yields.

One of the major disadvantages of use of AHF has been the inability to treat the product in a manner that would reduce or eliminate the potential for disease transmission. Recently all four commercial manufacturers received approval from FDA to begin marketing of heat-treated AHF. Although some manufacturers have data which indicate the process may reduce the transmission of viral diseases, there is no AHF product which has yet been proven to be entirely free of risk.

Table 23.-Manufacturers of Coagulation Factors Licensed for Use in the United States

Manufacturer	Factor VIII	Factor IX Complex	Anti-Inhibitor Complex
Alpha	x	x	
Armour	x	x	
Cutter	x	x	
Hyland	x	x	x
Immuno			x
New York Blood Center	x		

SOURCE: Grossman & Schmitt, 1984.

One liter of frozen plasma processed for AHF will yield approximately 200 AHF activity units. Based on market prices in mid-1984, the value of this product would be between $0.07 and $0.10 per activity unit, or between $14.00 and $20.00 per liter for non-heat-treated product. The heat-treated product sold during the same period for $0.11 to $0.16 per activity unit, or approximately $22.00 to $32.00 for the yield from 1 liter of frozen plasma. (It has been reported that the yield of heat-treated Factor VIII is slightly less than the yield of non-heat-treated Factor VIII from 1 liter of frozen plasma.)

The second major coagulation factor is Factor IX Complex, which is a product consisting of coagulation factors II, VII, IX, and X. Factor IX Complex is used in treatment of hemophilia B, as well as in treatment of some patients with inhibitors to Factor VIII. As with AHF, Factor IX Complex is measured in activity units and is prepared as a lyophilized powder which is reconstituted prior to injection.

Most of the U.S. market for Factor IX Complex is shared by two plasma fractionators, Cutter and Hyland. The total U.S. consumption of Factor IX Complex is estimated at approximately **130** million activity units per year. Based on a yield of approximately **400** activity units per liter, it takes 325,000 liters of plasma to meet this need. Based on market prices in early 1984, the value of Factor IX Complex was between **$7.8** million and $13 million.

The other coagulation factor product is "activated" Factor IX, or anti-inhibitor coagulant complex, for treatment of patients with inhibitors to Factor VIII. This part of the market is serviced by two companies, Hyland and Immune.

In addition to the manufacturers listed above, who distribute the products manufactured in their own processing facilities, the American Red Cross

has plasma fractionated into the various clotting factors by selected manufacturers. These plasma derivatives are returned to the Red Cross regional blood centers for distribution to hospitals and hemophilia treatment centers. Numerous suppliers and regional blood centers also purchase products for distribution to their local hospitals and hemophilia treatment centers.

Distribution channels for the coagulation proteins vary from region to region. Availability is often dependent on whether there is a hospital or hemophilia treatment center in a particular region. Most large urban areas have at least one major hemophilia treatment center that routinely stocks the various clotting factors.

Depending on the size of the region, patient requirements, and product preferences, numerous purchasing channels can be encountered. The hospital may solicit bids for the various factors required through its Purchasing Office in conjunction with the Pharmacy or Blood Bank, but there does not appear to be a standard as to which department should take responsibility for purchasing, inventory control, or distribution of coagulation factors within a hospital.

Depending on the institution, it could be assigned to the Blood Bank, Pharmacy, Purchasing Office, or Hemophilia Treatment Center. It is not uncommon for one company to receive the entire award for a l-year period for a particular product at a hospital or hemophilia treatment center. When numerous patients are treated at a hospital, the treating institution may require products manufactured by several manufacturers. To assist hospitals and reduce their inventory requirements, many institutions utilize the services of a local distributor or regional blood center, which maintains adequate supplies of each of the needed clotting factors.

In recent years, home care treatment of hemophiliacs has increased. At least one manufacturer, numerous distributors and pharmacies, and several regional blood centers have begun to supply these products directly to the patient at home. Orders are filled in response to instructions from the treating physician, and home care treatment has lifted the burden from the patient of having to visit the hospital each time a treatment is required. The regional blood centers, manufacturers, distributors, and pharmacies that distribute clotting factors to home care patients often provide the supplies needed to administer the clotting factors—which saves time, money, and effort in having to secure them from another source.

Some manufacturers will only supply end-users, such as hospitals or blood centers, or directly to patients. Other suppliers provide products to end-users, distributors, and other suppliers. Suppliers of coagulation factors vary from region to region, as does the availability of these products. Purchase and selection of a specific brand is often left to the patient, unless the physician specifies a particular brand.

Packaging, supplies, and availability, as well as price contribute to the numerous differences in the supply and use of the various clotting factors. Brand awareness of the product on the part of physicians, nurses, and patients often plays an important role in sales of various coagulation factors.

Brand loyalty is encouraged by manufacturers by supplying information at educational seminars and through direct communication with the physician and hemophilia nurse-clinician. Information is also provided directly to the patient by company representatives at many of the various national and local hemophilia meetings. Manufacturers provide a wide array of product sizes, and product preferences and loyalty are often based on the successful response a patient has had with the product in past treatment episodes, not on what manufacturers tell patients.

Immune Globulins

Immune serum globulins (ISG) account for approximately 10 percent of the total dollar volume of plasma derivatives distributed in the United States. A typical preparation of ISG will contain multiple antibodies to a wide variety of infectious agents.

ISG is available in either “normal” or “hyperimmune” preparations. The “normal” product is produced from the plasma of donors who have not been stimulated to produce elevated levels of specific antibodies. “Hyperimmune” ISG products are

obtained from donors with elevated levels of a specific antibody. This elevation may occur naturally, as with antibodies to the Rh blood type (Rho(D)) or hepatitis B, as a result of the donor's prior medical experience, or maybe obtained by injection of materials designed to produce an immune response in the form of antibody formation (319).

Specific types of ISG which are presently available in the United States include normal immune serum globulin, and hyperimmune globulins against hepatitis B, measles, mumps, pertussis, tetanus, rabies, varicella zoster, and RHo(D). All of these ISG products are available for intramuscular, not intravenous, injections. ISG is prepared as a 16.5 percent protein solution and distributed in vials ranging from 2 to 10 ml each.

In the United States, varicella zoster immune globulin (VZIG) is manufactured only by the Massachusetts Biologics Laboratory and is distributed primarily by the American Red Cross and other regional blood centers. Since this limited market drug was licensed, no other manufacturer has begun to produce it for distribution within the United States.

Intravenous gamma globulin is indicated for maintenance treatment of patients who are unable to produce sufficient amounts of IgG antibodies. Use of this product may be preferred to that of the intramuscular immunoglobulin preparations, especially in patients who require an immediate increase in intravascular immunoglobulin levels, in patients with small muscle mass, and in patients with bleeding tendencies in whom intramuscular injections are contraindicated.

Intravenous gamma globulin (IVGG) is currently produced only by Cutter, and is available directly from Cutter, regional blood centers, or distributors for purchase by prescribing hospitals and physicians. Immuno and Sandoz have applied for licensing of their IVGG products. The products under review by FDA are prepared in a lyophilized form, whereas Cutter's IVGG is prepared in solution. Manufacturers of some of these products are listed in table **24.**

Manufacturers of the various immune globulins distribute their products through many channels.

Table 24.—Manufacturers of Selected Immune Globulins for Use in the United States

Manufacturer	ISG	IVGG	RHoD	HBIG	VZIG
Abbott			x	x	
Armour	X		x		
Connaught/BCA			x		
Cutter	X	X	x	x	
Hyland	X				
Immuno		X[a]			
KABI			x		
Massachusetts Biologics Laboratory					X
Merck Sharp & Dohme				X	
New York Blood Center	X				
Ortho			X		
Sandoz		X[a]			

[a]Application for licensing pending before FDA as of May 1984.

KEY: **ISG**: immune serum globulin; **IVGG**: intravenous gamma globulin; **RHoD**: anti-RH antigen immune globulin; **HBIG**: hepatitis B immune globulin; **VZIG**: varicella zoster immune globulin.

SOURCE: Grossman & Schmitt, 1984.

While almost every hospital utilizes some or all of the immune globulins, there is usually no central distribution or supply network as is available for normal serum albumin or coagulation factors. Some manufacturers, such as Ortho, have a large share of a specific market such as for RHo(D), but they do not sell other plasma derivatives in the United States.

Immune globulin products are routinely delivered 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.

Many manufacturers have their own sales representatives, who contact individual physicians to encourage the ordering of brand-specific products. Within the hospital, these products may be ordered by the Pharmacy, Purchasing Office, Blood Bank, or by a special user department. The department requesting the product often specifies which supplier or manufacturer should be used, based on services and product results in the past.

Annual bidding for each immune globulin product is not as prevalent as for other human plasma derivatives, but is gaining. Usually, an award is made for one company's product, and supply has not been a factor since all manufacturers usually have adequate inventories.

Many other manufacturers of immune globulins offer various products and numerous customer advantages, including low prices, well-located distribution outlets, and ease of ordering. The two most important advantages are availability at the time the product is needed and pricing.

Reagent Products

Plasma not suitable for further manufacture into injectable is available for use by reagent manufacturers. Plasma for this market is available from a variety of sources, including regional blood centers, hospital blood banks, plasmapheresis collection centers, and plasma fractionators.

The number of manufacturers within the United States requiring plasma for reagents is quite large, and each one has strict requirements for the plasma that it obtains. Usually, human plasma destined for reagent use is sold to plasma dealers who routinely supply laboratory reagent manufacturers and are familiar with the necessary specifications. Many of these dealers also provide a wide array of animal proteins to the same laboratory reagent manufacturers.

Each manufacturer of reagent products provides its sources of human plasma with the requirements that must be followed in the preparation of the material. These strict manufacturing specifications often limit the sources of plasma to a highly select group of hospitals, plasma collection centers, and bulk product manufacturers. Plasma suppliers that specialize in meeting the reagent manufacturer's specifications usually maintain a long-term relationship with these manufacturers. Some collection centers specialize in preparation and segregation of plasma from donors with special or rare characteristics for use by selected reagent manufactures.

Other Plasma Derivatives

At the present time, many proteins found in human plasma are being evaluated and studied for their therapeutic value. Proteins such as Alpha I Antitrypsin, Antithrombin III, Factor XIII, Fibronectin, Tissue Plasminogen Activator, von Willebrand Factor, and Interleukin-2, as well as new immune globulin preparations, are being evaluated by numerous commercial and nonprofit research facilities. The American Red Cross and the Michigan Department of Public Health are jointly evaluating as a new plasma derivative a Factor IX Concentrate depleted of Factors II, VII, and X; and a concentrate of C1 Inactivator (373).

Several new plasma derivatives have been licensed for use in other countries and will, after passing the necessary testing, be licensed in the United States. Some of these products are: 1) Antithrombin III, currently marketed in Europe by Behring (Germany) and Kabi (Sweden); 2) Factor XIII, currently available in Europe by Behring (Germany); and 3) Fibrin Tissue Sealant (Tissell), currently marketed in Europe by Immuno (Austria) and projected to be available in the United States in 1985.

Costs of Major Plasma Derivatives

As already discussed, the market structure for plasma derivatives differs substantially from that for whole blood. However, the voluntary collectors compete with the commercial sector when marketing plasma products. Prices charged by selected not-for-profit blood centers are shown in table 25. Current retail prices for Factor VIII in the not-for-profit centers range from $0.10 to $0.147 a unit for non-heat-treated Factor VIII and higher for heat-treated Factor VIII. Prices charged by hospitals to patients are reported to range from $0.09 to $0.26 per unit in the United States (99; 464). 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, although "average" consumption can be a misleading figure.

Hemophiliacs can require a large infusion of Factor VIII for surgery, including minor surgery. Needs also vary for mild, moderate, and severe hemophiliacs. In addition, from 10 (99) to 15 (76) percent of hemophiliacs have inhibitors to Factor VIII and require anti-inhibitor coagulant complex, which can cost from $0.70 to $1.00 per unit (99).

Federal activities in support of hemophiliacs were discussed in chapter 2. While provisions for hemophilia care have improved in the last decade, coverage for coagulation proteins on an out-

Table 25.—Representative Blood Center Prices for Plasma Derivatives

Major blood derivatives		Blood Center: Goldman (Okla.)	S.E. La.	Sacramento	Central (Pittsb.)	NYBC[a] List	NYBC[a] Actual
Serum Albumin 5°/0	250 ml	34.1OF			28.00	41.00	31.00
Serum Albumin 5°/0	500 ml	67.65F			55.65	82.00	62.00
Serum Albumin 25°/0	20 ml				20.00		
Serum Albumin 25°/0	50 ml	35.20F	31.00		28.00	41.00	31.00
Serum Albumin 25°/0	100 ml			*75.00*	*55.65*	82.00	62.00
Plasma Protein F.	250 ml			*36.00*	*27.35*	41.00	31.00
Plasma Protein F.	500 ml				*54,35*	82.00	62.00
Factor VIII		0.132iu C			0.10iu	0.11 N	0.11
						0.147A1	0.147
						0.1 IAr	0.11
						O.1O4C	0.104
						O.1O8H	0.108
Factor VIII, (Heat-treated)		0.165iu H				0.187A1[b]	0.187
						0.145Ar	0.145
						0.142C	0.142
						0.129–0.153H	0.129–0.153H
Factor VIII Anti-Inhibitor Complex	200-600 FECU	0.77iu FB				0.75FB	.75
Factor VIII Inhibitor Complex	200-600 FECU	1.22H				1.01 H	1.01
Factor II, VII, IX, X complex	500 u vial	57.20C		62.50	0.12iu	0.066A1	0.066
						0.057Ar	0.057
						0.065C	0.065
						0.113H	0.113

Legend: AI =Alpha Therapeutics product; Ar=Armour product; C= Cutter product; F= Fenwal product; FB = FEIBA product; H = Hyland product, N = New York Blood Center product.
Where no letter is given, product name was not specified.
[a]Through June 30. 1984. Price includes New York Blood Center service fee for development and maintenance of data management and hemophilia research project. and hemophilia home care service.
[b]Prices may be unrealistic because NYBC does low volume in this product. Prices range from 0.11 iu (Cutter) to 0.165 (Alpha).

SOURCE: Grossman & Schmitt, 1964

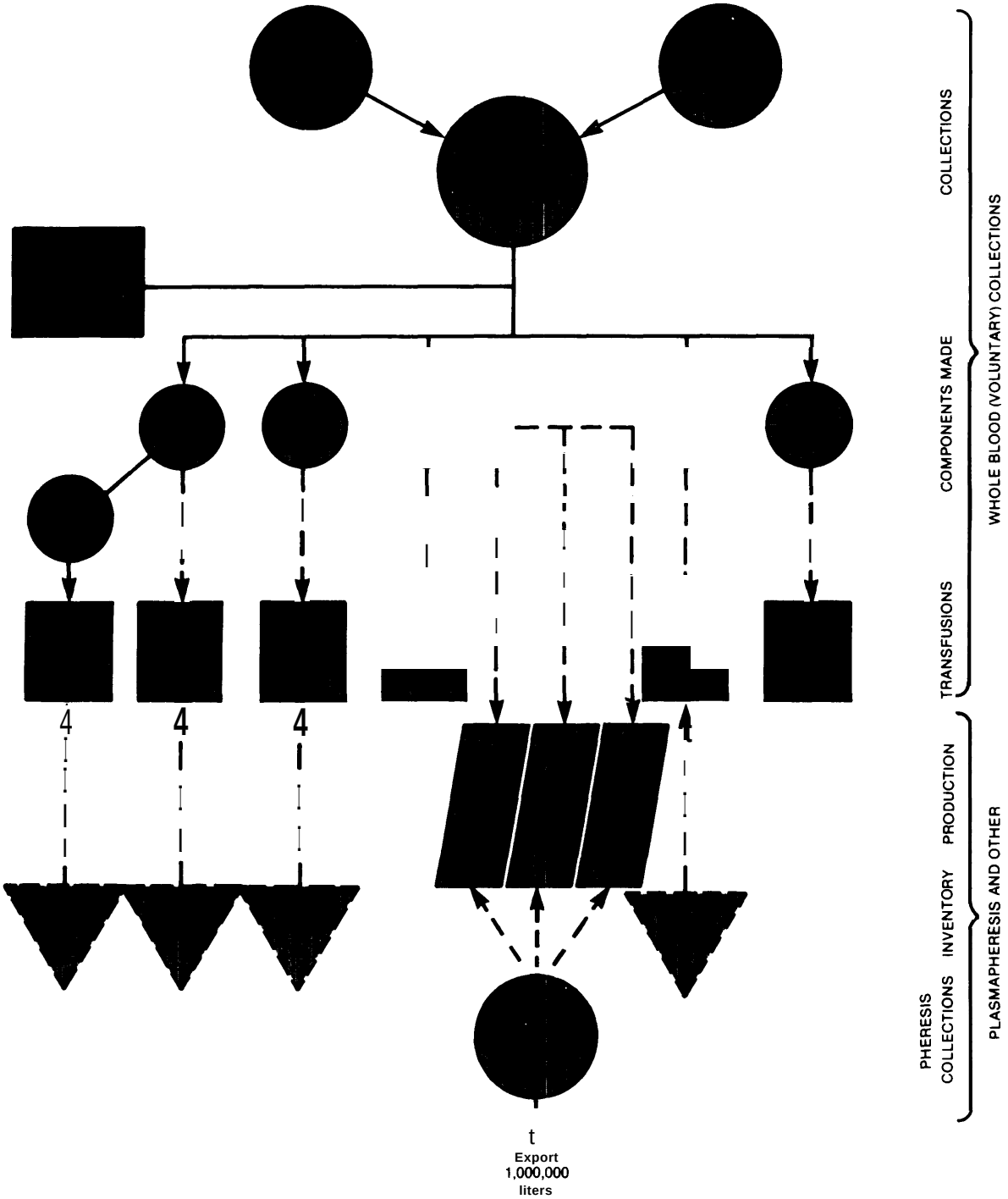
patient basis varies widely, and they are often not covered because they are regarded as drugs rather than biologics. When they are covered, copayment provisions can burden patients. Pharmaceutical companies that distribute Factor VIII sometimes ignore the copayment requirement for individual hemophilia patients.

The price of albumin has not been challenged per se, but some have encouraged the use of less expensive alternatives for volume restoration (see ch. 5, pt. 4). A 12.5 gram dose of albumin, prepared by a commercial fractionator and purchased from a blood center, cost approximately $32.00 in 1984. In 1982, the cost from commercial manufacturers was $27.40 (464).

CONCLUSION

U.S. blood resources consist of two distinct sectors, a voluntary whole blood system and a commercial source plasma industry (fig. 8). Human blood is the common denominator, but there are distinct differences between the two sectors in donor populations, recruitment policies, type of blood collected, markets (domestic v. international), indications for use, and Federal policy attention and directives. Even the acquisition and use of the products of these two sectors differ. Whole blood and its components are ordered and monitored through blood banks and transfusion

Figure 8.—Flow of the Nation's Blood Resources, 1980



[a]No question on the ABC National Blood Data Center Survey for this value. Number shown is the difference between total collections and mobile collections.
[b]No question on the survey for this value. An unknown quantity of whole blood, not made into components, was screened out (because of hepatitis B or other complications) or lost/broken during handling.
[c]Units of platelets were derived from plateletpheresis procedures. Platelets transfused include apheresis figures.

SOURCES: Figure adapted from Surgenor and Schnitzer/ABC (1983). *Whole blood figures:* Surgenor and Schnitzer/ABC (1983). *Plasmapheresis figures:* Reilly, personal communication, 1983; Rodell personal communication, 1983.