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Future Direction;

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PART 1: VOLUNTARY V. COMMERCIAL APPROACHES

Introduction

Federal policy attention in the past has concentrated on the whole blood collection process, spurred by differences in the safety of whole blood from voluntary v. paid donors. Currently, the distinction between voluntary and paid whole blood or blood component collections has been maintained through their labeling 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 (21 CFR pt. **640),** but does not apply to source plasma or plasma derivatives (21 CFR pt. 606.120).

Assurances of the safety of plasma and plasma derivatives have been pursued through regulatory policies of the Food and Drug Administration (FDA), which has spelled out donor screening and laboratory testing requirements (21 CFR, pts. 640.60-640.76). pooling of large amounts of plasma from individual donors is necessary for the efficient processing of plasma into plasma derivatives. Together with the donor and laboratory screening tests that have been applied, these technologies have resulted in the situation where there are no substantial differences in the safety of plasma derivatives whether they are derived from voluntary or commercial sources of blood / plasma.

But the availability of products derived from human tissues may also be influenced by criteria other than whether the market has resulted in a safe, readily available product, as witnessed in current legislative efforts to prohibit profit-making in systems for collecting and distributing organs (e.g., kidneys, livers and hearts) and other tissues (e.g., bone, skin and corneas). Thus, another viewpoint on the issue of voluntary v. commercial sources is, regardless of how well the present dual system is working, whether or not public policy should steer blood resources to an all-volunteer supply.

An additional consideration in analyzing the adoption of this type of public policy is whether or not the United States and other countries should be self-sufficient in resources that depend on human sources. Much of the self-sufficiency argument has been made in the context of exploitation of donors in developing nations, whose plasma was then used by fractionation companies for products used in the developed nations (250). In 1975, at the Twenty-Eighth World Health Assembly, the World Health Organization issued a resolution urging its member States "to promote the development of national blood services based on voluntary nonremunerated donation of blood, " and "to further study the practice of commercial plasmapheresis including the health hazards and ethical implications, especially in developing countries" **(595).**

Currently, however, at least as far as U.S. plasma fractionation and use of plasma derivatives are concerned, the situation is such that U.S. plasma sources constitute the world's single largest source of raw plasma and plasma derivatives, and the primary issue among nations that use U.S. fractionated derivatives seems to be self-sufficiency per se, regardless of the source of the plasma derivatives. In addition, these importing nations seem more concerned now with the safety of U.S. plasma derivatives (because of AIDS, see below) than with the ethical implications of importing these blood products.

A strict self-sufficiency policy would also mean that international trade in voluntary blood products, as well as in commercially obtained products, would be discouraged. Thus, for example, the sale of excess red cells accumulated by some European countries in collecting whole blood for plasma-derivative production to the New York Blood Center (and commonly referred to as "Euro-blood") would also be discouraged.

On the issue of self-sufficiency, one possible outcome of the AIDS controversy is that it is forcing nations currently dependent on U.S. plasma to look into the question of whether or not they should and could be self-sufficient. Currently, only the United Kingdom officially prohibits the import of U.S. plasma, but several western European countries have recently investigated their imports of U.S. plasma and have urged their own fractionators to show cause why they must continue such importation. Since an immediate ban on U.S. imports would seriously curtail the availability of Factor VIII concentrates, these countries have not taken any official action (466).

Voluntary Efforts in the Plasma Sector

There have been some forays into plasma collection and fractionation by the voluntary sector. In the mid-1970s, at least one voluntary blood bank conducted a small-scale plasmapheresis program for over 4 years, and although it was not economically feasible to continue, it was found that people would donate plasma voluntarily on a regular basis (402).

Some plasma fractionation activities also exist in the voluntary sector, and a few years ago the Red Cross attempted to build a fractionation plant with one of the commercial fractionators. The States of Michigan and Massachusetts maintain plants with capacities to fractionate 50,000 liters of plasma a year, and the Massachusetts plant is currently the sole source of herpes zoster immune globulin in the United States (see ch. 3, pt. 2). The New York Blood Center also maintains its own 350,000 liter/year plasma fractionation plant to fractionate its own and some Red Cross plasma, which required an investment of approximately $12.5 million **(306).**

In 1978, the American Red Cross negotiated an agreement with Baxter-Travenol to jointly fund the construction of a fractionation plant for plasma products. The cost of the plant was estimated at $45 million (406). Under the agreement, each organization would have been entitled to half the production capacity of the plant, but each organization would have handled its own acquisition of plasma and distribution of the plasma products. The plant was to have an annual fractionation capacity of 1 million liters, and industry sources estimated that the joint venture would have resulted in control of 30 to 44 percent of the U.S. plasma fractionation business (103,134).

The American Red Cross had requested a business review in April 1978 by the antitrust division of the Justice Department in regard to the legality of the joint venture's effect on substantially lessening competition in the plasma fractionation industry. In May 1978, the American Blood Resources Association submitted comments arguing that the joint venture would violate the antitrust laws by eliminating actual and future competition between the Red Cross and Baxter-Travenol (328), but the Justice Department announced in October 1978 that it would not challenge the proposed venture.

The Justice Department discounted the lessening of potential competition on the grounds that the Red Cross lacked the requisite technological ability to enter the fractionation business alone. It also dismissed the notion of a lessening of actual competition because: 1) Red Cross and Baxter-Travenol were clearly not actual competitors in fractionation at the time the venture was being considered, and 2) although the market shares of the Red Cross and Baxter-Travenol would have been significant enough to violate the Court's interpretation of "reasonable," the structure of the joint venture clearly delineated plasma collection and product marketing as separate responsibilities of each organization (328,391). Thus, the department concluded that competition in the plasma industry would continue and that the joint venture should be allowed to proceed.

In March 1979, the Red Cross and Baxter-Travenol announced the agreement (406).

During June-December 1979, West Germany began a procedure to remove the German Red Cross's tax-exempt status on income from manufacture and sale of plasma derivatives through its blood donor service (317,329). In June 1981, the German Minister of Finance concluded that such income should be taxed and treated as a profitable business activity because of the competitive nature of the industry, distinguishing between blood collection and the "secondary step of fractionation" (438). The decision was made retroactive to January 1, 1981 (320).

Although no official statement to the effect was made, the joint venture may have raised similar issues for the American Red Cross. The issue would have been "whether plasma collection, fractionation, sale and other distribution constitute a trade or business which is sufficiently related to the Red Cross's exempt purposes that that business does not generate unrelated business income" (329). Traditionally, the provision of blood to health care facilities at the lowest possible price has been regarded as a charitable service to the public, and plasma has been included. The joint venture may have provided a new answer to one of the Internal Revenue Service's standard tests for taxable activities; i.e., whether or not the activities in question were "of a kind regularly carried on for profit" (Rev. Rul. 66-323).

In late 1979, the Red Cross and Baxter-Travenol terminated their agreement, citing general economic conditions as the cause. The Red Cross' public relations office gave increases in construction costs of one-third ***over*** the budgeted amounts, inflation, and the increase in interest rates, as the relevant factors in the decision to shelve the project. Today, the Red Cross continues to contract with independent fractionators for the necessary service. Recently, the Red Cross entered into an agreement with Travenol Laboratories for the fractionation of Red Cross-provided plasma by Travenol's Hyland Therapeutics Division. Under the agreement, Hyland will increase its fractionation for the Red Cross on a fee-for-service basis to four times the volume of plasma fractionated for the Red Cross under current agreements, and Hyland will provide the Red Cross with a pilot plant facility for research on new orphan products, to be developed by the Red Cross under Travenol's FDA license.

In Canada, all blood and most plasma, with the exception of a small amount of plasma collected for production of plasma products, are collected by the Canadian Red Cross (CRC) from volunteer donors. Although the Canadian national blood policy is still under development, all activities related to the blood program are guided by principles which have been followed since the early 1970s. The current version of the principles was adopted by the Ministers of Health (one Federal, ten provincial, and two territorial) in November 1980. As health services are the constitutional responsibility of the Provinces, their endorsement has considerable authority. The policy, however, is not incorporated in either Federal or Provincial law.

Further, the Ministers of Health have conferred on the Canadian Blood Committee (CBC) the responsibility to "direct the Canadian blood system on their behalf" in accordance with the four guiding principles. The members of the CBC are representatives of 13 governments (Federal, Provincial, and Territorial), and are funded equally by the Federal government and the Provincial and Territorial governments (337).

The "Four Principles" approved by the Provincial Ministers of Health are (106):

1. to protect the voluntary donor system by enhancing the opportunities of Canadians to voluntarily donate a gift for society's general benefit and by responsibly managing that resource;
2. to ensure self-sufficiency of blood products by reducing Canada's dependence on foreign sources of blood products supply, particularly those that rely on purchased plasma for raw material;
3. to ensure gratuity of blood products by reinforcing the Canadian tradition whereby no payment is made for a donation of blood and/or plasma and no specific charge is made to recipients of blood and blood products; and
4. that a Canadian nonprofit policy be maintained and that any charge to recover more than the real cost of producing a blood fractionation product for Canadians in Canada should be considered profit.

The first three principles were articulated in 1973, and the fourth was added in 1980 after Connaught Laboratories, one of the two fractionators serving the CRC, changed its status from nonprofit to commercial. The reason given for adding the fourth principle was that "it was consid-

ered that the Canadian public would not accept the 'exploitation' of plasma donated voluntarily to the CRC" (147).

The second principle was based on a national goal of self-sufficiency, especially with respect to plasma fractions. The third principle, which denies any specific charge for blood, means that patients or their insurers are not billed by CRC for any cost of providing blood products. They may, however, be billed for the service of cross-hatching if provided by an institution (hospital or private laboratory) other than the CRC. (The Canadian Blood Committee sets the prices of blood fractions.) The CRC views the blood program as an expenditure. The Blood Transfusion Service recovers the costs of recruitment, processing, etc., through direct grants from the Provinces and funding from the Canadian Red Cross Society. (See subsequent discussion on finances of the Blood Programmed.)

The nonprofit / no-charge principles apply to human products for therapeutic use, not to diagnostics. However, CRC itself produces diagnostic reagents for its own use and distributes some histocompatibility trays to other Canadian laboratories free of charge. (The human leukocyte antigen (HLA) trays distributed in 1982 at no charge had an estimated market value of $556,140 at average U.S. prices.)

Currently, there are two Canadian firms which pay donors for plasma. Their products are commercially marketed. The first is The Winnipeg RH Institute, Inc., which is associated with the University of Manitoba. It is a nonprofit organization which primarily produces immune globulins and is also licensed by the U.S. FDA as a source plasma location. The second is BioResources, Ltd., of Halifax, Nova Scotia, which collects plasma principally for manufacture of diagnostic reagents, some immune globulin products, etc.

Plasma is fractionated for the CRC by Connaught Laboratories Ltd., of Toronto, Ontario, and Cutter Laboratories, of Clayton, NC. Each receives 70,000 to 75,000 liters per year. New facilities in Winnipeg (RH Institute) and Montreal (Institute Armand Frappier) will allow fractionation of all CRC plasma in Canada; each will process 50,000 to 60,000 liters annually.

The blood collection system in Canada is administered by the Blood Transfusion Service (BTS) of the Canadian National Red Cross and is coordinated from a national (blood transfusion service) office in Toronto. The BTS includes 17 regional transfusion centers within 10 provincial divisions. The technical operations are directed nationally, but blood donor recruitment is the responsibility of each division. There is a national Blood Donor Recruitment Program which provides information, resources, etc., but the national division is not responsible for regional recruitment. The regional transfusion centers collect and distribute blood and blood products.

In addition, the BTS operates the National Reference Laboratory (NRL), which also functions as the World Health Organization's National Blood Group Reference Laboratory. The NRL's activities include reagent production and quality control, hepatitis testing, HLA typing tray production and distribution, and a variety of reference and investigational testing.

In 1982, there were 8,928 clinics throughout Canada. In the Canadian system, "blood donor clinics" (bloodmobiles, blood drives, blood collection sites, etc.) are divided into three types:

- Region 1: clinics are permanent sites at or close to a regional transfusion center. These represent 48 percent of the total number of clinics.
- Region 2: clinics are mobile clinics close enough for blood to be collected, delivered to a center, and processed within 12 hours of collection. These constitute 42 percent of all clinics.
- Region 3: clinics are mobile clinics beyond 12 hours of a regional center, and make up the remaining 10 percent of clinics. Blood collected from Region 3 clinics is used for the extraction of those components whose shelf life before processing exceeds 12 hours.

In 1982, the Blood Transfusion Service of the CRC collected 1,129,159 units of blood. Of these, 855,765 units were transfused as whole blood or red cell concentrates (There was a 24.2 percent national outdate rate for collected whole blood and red cells in 1982.) Ninety percent of the whole blood collected was processed into components.

Plasma recovered from whole blood equaled 797,922 units, or approximately 160,000 liters. In addition, 7,831 voluntary plasmapheresis donations yielded over 3,900 liters of plasma. About 51,600 liters of plasma were transfused, and 153,650 liters (including 113,267 liters of fresh-frozen plasma) were available for fractionation (107).

The CRC meets all Canadian requirements for blood and blood components, other than plasma fractions. The only major import is Factor VIII concentrate, which is imported at the rate of 20 million to 22 million activity units per year at a value of approximately $2 million in Canadian dollars. Other products imported in relatively small amounts are specific immunoglobulins to varicella zoster, hepatitis B, tetanus and rabies, and the activated Factor IX Complex. CRC plasma sources supply all albumin, normal Factor IX Complex and pooled immune serum globins, and about 20 million units of Factor VIII (147).

Both Canada and the United States collect approximately the same amount of whole blood from voluntary donations per capita. Both countries separate the majority of whole blood into components, although Canada processes a higher percentage (90 v. 77 percent) of the blood available after whole blood transfusions. Perhaps the most significant difference is the percentage of plasma which is prepared as fresh-frozen plasma (FFP). Plasma must be in the fresh-frozen state to be useful for Factor VIII preparation. Of the plasma prepared from whole blood donations, the United States prepared only 33 percent in the fresh-frozen state (in 1980, the last year for which national statistics are available), while Canada prepared 72 percent as fresh-frozen plasma (for 1982). A comparison of U.S. and Canadian plasma management by the voluntary sector is summarized in table 45.

The Blood Transfusion Service of the Canadian Red Cross Society is supported in part by the government and in part by CRC fundraising efforts. The Provinces fund the blood program directly by grants for operating budgets and also by payment per item for fractionation products supplied to hospitals. In addition, the Canadian Red Cross funds the blood program along with its other charitable activities, such as international disaster relief, veterans' services, and safety services. The Canadian Red Cross Society programs and budget are subject to the review and approval of the Canadian Blood Committee.

About 60 percent, or $80,959,000, of the Canadian Red Cross's total expenditures ($135,249,000) for 1982 was spent on the blood program. These expenditures include all aspects of the blood program; i.e., all 10 regions, the National Reference Laboratory, national BTS offices, and the Blood Donor Recruitment Program. There was a deficit of $451,000 in 1982 (108).

In 1983, the Canadian Red Cross instituted a revised system of accounting in order to provide for the large amount of working capital needed for operating the blood program. The new system provides for separate financial reporting for the activities of the BTS, the national BTS office and fractionation operations. Each dollar is budgeted in the following proportions:

$0.33	for collections
0.24	for processing
0.14	for administration of centers
0.11	for donor recruitment
0.07	for the national office
0.07	for distribution
0.04	for the National Reference Laboratory
$1.00	Total

Prospects for Further Voluntary Sector Involvement in Plasma Operations

Voluntary sources for all products made from human blood and plasma remain as the ideal goal for many, and volunteers are relatively untapped sources of plasma, perhaps even on the sustained basis that is the norm for the commercial source plasma industry. Furthermore, volunteers need not be the exclusive source of plasma for national policies that stress the voluntary approach, as witnessed by Canada's experience. However, other factors make it unlikely that a policy will be pursued to make the voluntary sector the exclusive or even dominant collector of plasma as well as whole blood in the United States.

Table 45.—A Comparison of U.S. and Canadian Plasma Management

	United States—1980	Canada—1982
Voluntary whole blood donation per 1,000 population	47 units	46 units
Whole blood collected	10,863,442 units[b]	1,129,159 units
Paid donations	233,127	0
Voluntarily donated blood	10,630,315	1,129,159
Whole blood transfused	1,930,081	77,517
Units available whole blood	8,700,234 units	1,051,642 units
Percent whole blood processed into components	77%	90%
Percent whole blood transfused	180/0	7%
Maximum recoverable plasma from volunteer donor blood left after whole blood transfusions	1,740,047 liters	210,328 liters
Estimated plasma available from separated whole blood[f]	1,631,780 liters	202,585 liters
Fresh-frozen plasma produced[g]	440,377 liters	143,433 liters
Other plasma produced	878,536	56,151
Total plasma produced	1,320,510 liters	199,584 liters
Percent plasma prepared as FFP[h]	33 "/0	72°10
Donated source plasma[i]	21,722 liters	3,900 liters
Voluntarily donated source plasma per 1,000 population	96 ml.	160 ml.

[a]Calculated as units whole blood voluntarily donated/population:
U.S. population (1980) 227,020,000
Canada (1982) 24,438,000
Source: U.S. Bureau of the Census, World Population 1979, Recent Demographic Estimates for the Countries and Regions of the World, 1980; Demographic estimates for countries with 10 million or more, 1981; and unpublished data.
[b]Whole blood figure does not include Euroblood.
[c]Calculated as units RBC processed/units whole blood voluntarily donated; units RBC processed U.S.: 8,158,898 units, Canada: 1,012,926 units.
[d]Calculated as units whole blood transfused/units whole blood donated.
[e]200 ml (or 0.2 liters) of plasma is the industrywide standard for plasma recovered from a unit of whole blood. Source: R. Reilly, personal communication, Jan. 5, 1984.
[f]Calculated as (units RBC processed) x (0.2 liters/units).
[g]Recovered plasma must be in the fresh-frozen state to be useful for Factor VIII production. Source: AABB, *Plasma Products: Use and Management*, p. 17, 1982.
[h]Calculated as liters fresh-frozen plasma produced/liters plasma produced.
[i]Recovered plasma: plasma obtained as derivatives of whole blood donation. Source plasma: plasma obtained from plasmapheresis procedure (yield: approximately 600 ml/donation); U.S. figure does not include the approximately 6 million liters of source plasma collected annually by commercial organizations.

SOURCES: **U.S. data source:** Surgenor and Schnitzer/ABC, 1982. **Canada data source:** Canadian Red Cross Society Blood Transfusion Service, 7982 *Statistic/ Report,*

One consideration is whether the voluntary sector could meet the U.S. demand for plasma derivatives. Drees has estimated that an additional 20 million whole blood donations would have to be made to replace the 5 million liters of plasma collected by commercial collectors (at the time of his estimate), assuming a 250 ml plasma yield per volunteer donation of 500 ml of whole blood (165). This would have required tripling the approximately 10 million units of whole blood collected at the time of his estimates. An equivalent amount of plasma collected by plasmapheresis would need approximately 8.34 million collections, based on a yield of 600 ml of plasma per procedure.

U.S. plasma sources, however, also supply a large part of the world market, and not as much plasma would be needed for the U.S. market alone. However, it has been argued that U.S. sales abroad at prices as high as three times the U.S. price for Factor VIII help keep domestic prices down (7), and a self-sufficiency policy that would discourage international sales of U.S.-derived plasma products might reduce this beneficial impact on U.S. prices. It could be argued that this salutary effect on U.S. prices is due to "price gouging" abroad, but the other side of the coin is that these other users are paying the "market price" for products they do not produce in sufficient quantities themselves.

There obviously is no resolution of these conflicting opinions on the "morality" of selling plasma products at prices which can be obtained in the market. Of interest to this essentially unresolvable debate is that, once plasma is processed into derivatives, they are treated as commodities, or perhaps more accurately, are treated in much the same way as prescription drugs by both manufacturers and purchasers. This is true especially for albumin (whose marketing is similar to that for generic drugs) and increasingly true even for Factor VIII concentrates, and nonprofit organizations are commonly involved in marketing both nationally and internationally (see ch. 3 on the plasma sector).

Marketing of plasma derivatives by both profit and nonprofit organizations in direct competition with each other also points to the fact that, once past the stage of plasma or whole blood collections, the profit and nonprofit sectors have become more intertwined over the past decade. This is largely due to the increasing use of component therapy and the excess plasma that has become available from the voluntary sector. So any fundamental changes that occur in the plasma derivatives industry will cause problems for the voluntary sector as well.

Voluntary organizations may also be unwilling to become the major suppliers of plasma and plasma derivatives. Aside from the problems of establishing and maintaining an adequate donor supply, costs for starting up or retooling plants for plasma fractionation are substantial, as witnessed by the abandoned Red Cross/Baxter-Travenol proposed joint venture.

Even if present commercial fractionators continued to fractionate plasma that would come primarily from voluntary sources, there is still the question of the medium- and long-range health of the plasma derivatives industry. Albumin is no longer the driving force in the derivatives market and sales are very competitive. As noted earlier (see ch. 3), the market is not large compared to other industrial sectors, and major companies have left the industry in recent years.

The major factor, however, in determining the future of the plasma derivatives industry is the real chance that, by the end of the century, plasma as a source of current biological proteins will be (largely) replaced by recombinant DNA and hybridoma technologies (see ch. **6).** These developments would affect not only the source plasma industry, but also plasma fractionators, some of whom are sponsoring biotechnology R&D in anticipation of these events. Thus, biotechnology currently has two major impacts on the issue of voluntary v. commercial supplies of source plasma and plasma derivatives. First, it makes the future prospects of this sector of the blood services complex sufficiently doubtful so that no planned movement toward a voluntary system can be expected. Second, however, biotechnology shows sufficient promise that, 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. commercial policy debate moot.

PART 2: ORGAN AND TISSUE BANKING

Introduction

In a recent volume on the role of blood bankers in tissue and organ preservation, one conclusion was that: "Within a decade after the end of this century, it is unlikely that there will remain more than a few vestiges of conventional blood banking as it exists today. There area number of health service areas into which blood centers can diversify, but one of the most obvious is tissue banking" **(376).**

The idea that blood bankers are particularly well-suited to have a central role in preservation and distribution of organs and tissues other than blood is not entirely novel. In its first paragraph, the decade-old National Blood Policy speaks not only of "improvement in the quality of blood and blood products, " but also of "development of an appropriate ethical climate for the increasing use **of *human tissues for therapeutic medical pur-***

poses" ((179); emphasis added). A year later, in 1975, an editorial in ***Transfusion*** (299) asked: "Are blood banks to become tissue banks?"

Advances in surgical techniques and development of more sophisticated immunological agents to combat rejection problems have made it possible to transplant a host of solid organs and tissues, including the heart, lungs, kidney, liver and pancreas. Some transplantable substances, like bone marrow, are akin to blood and its components because they are renewable substances which can be provided by living donors. Organs such as hearts, livers, and lungs are procured from the bodies of people who have been declared dead on the basis of total and irreversible loss of all brain functions, but whose heart and lungs continue to be supported by artificial means, allowing the organs to be perfused. For tissues, including corneas, skin, and bone, potential donors include almost any dead body. Clinically, tissue donors are unlike organ donors in that tissues can be taken after the donor's heart has stopped beating and the actual retrieval is technically less rigorous.

Although the nature of the donor and the techniques and methods used to arrange for collection, storage, and distribution vary among the different types of organs and tissues, many features of the process have much in common with the blood banking enterprise. Finding donors, storing and inventorying products, assuring safety through a variety of screening tests, distributing the product, and recovering costs are all features common to blood banking and tissue and organ banking.

The blood bank's traditional role is also a key element in many transplant procedures. One dramatic example of the need for blood is in the area of liver transplants. At the University of Pittsburgh, where this procedure was pioneered by Dr. Thomas Starzl, liver transplants require about 3,000 to 4,000 units of blood from the hospital blood bank's annual dispersal of about 130,000 units (229). The strain on the blood bank is not so much the volume of blood needed (open heart procedures at the same center account for five times as much blood usage) but rather the unpredictable nature of the need. When a liver from a brain-dead donor is found, blood must be available within 4 to 6 hours—on occasion as much as 100 units.

While the need for this much blood is the exception, routine requirements for a range of blood products are nevertheless rather substantial. One study of 60 adult first-time liver transplant recipients revealed the following mean intraoperative and postoperative requirements per patient: red blood cells, 42 units; fresh-frozen plasma, 39 units; platelets, 19 units; cryoprecipitate, 8 units (283). According to Richard Crout, the director of the Office of Medical Applications of Research of the National Institutes of Health: "The amount of blood required is much greater than most people realize. It is an important limitation on expansion of this new technology—a major reason why local hospitals aren't about to get into transplanting livers" (229).

The Current Scene

The modem era of transplantation began in the 1950s with the first attempts at kidney transplantation. These initial procedures were limited to identical twins, whose common genotype obviated the problem of rejection. With the development of immunosuppressive drugs to combat such problems, surgeons were soon able to utilize less closely related living donors and eventually, cadaver donors. In 1963 the first liver transplant was performed, and in 1967, the first heart transplant (389). To date, there have been approximately 500 heart transplants performed in the United States and about 600 liver transplants worldwide, most of them in this country (278). In 1983 alone there were 6,138 kidneys, 163 livers, 172 hearts, 37 heart-lung combinations, and 150 pancreatic transplants performed in the United States.

With burgeoning interest in transplantation in the late 1960s, it became apparent that the law was lagging behind medical advances. Law reform bodies and professional associations drafted a model statute to clarify the legal status of organ donation and transplantation, codifying the common-law powers of an individual to donate body parts for use after death. By 1971, all State juris-

dictions save one had adopted the Uniform Anatomical Gifts Act (UAGA) as recommended by the National Conference of Commissioners on State Laws (Kentucky joined the rest in 1977) (362).

The UAGA allows people to make known their intention to become organ donors by signing wallet-sized documents they can carry with them. In addition a number of States have made similar provisions to provide evidence of such intent on drivers' licenses. The UAGA also allows family members, in the absence of any contrary intent, to consent to organ removal on behalf of their relatives who have been declared brain-dead. The act, in addition to specifying who may give third-party consent for organ donation, also spells out an important division of labor: in order to avoid any conflict of interest, physicians responsible for declaring that the donor is dead may not be the same ones involved in the transplant procedure.

The Procurement System

A network of approximately 110 independent and hospital-based procurement agencies exists to coordinate distribution of organs. There are about 360 people in the country whose full-time work involves coordinating organ donation (278). The procurement centers have also been grouped into regional networks and have established computer and phone links. For example, the Southeast Organ Procurement Foundation is one such network, consisting of 30 centers. In addition to transplant coordinators, surgical transplant teams, intensive care unit personnel, patients, and the families of donors are also involved. To date this patchwork system has worked remarkably well, but many predict that without further refinements it will be unable to meet the increasing demand for organs suitable for transplantation (152).

One key actor in the transplant process is the transplant coordinator. This person, often a nurse or social worker, is responsible for maintaining a liaison between the transplant team and the family and caregivers of the potential donor. Most often the potential donor is identified by a neurosurgeon or neurologist upon declaration of brain death or by a nurse in the intensive care unit. The coordinator is often the person who must broach the sensitive issue of organ donation to a grieving family, explaining the ofttimes disconcerting concept of "brain death. " It has been estimated that only 1.6 to 3.5 percent of people dying in acute care settings are potential organ donors; most often these are people who have sustained traumatic injury (64). Since many fewer actually become donors, it is difficult to build ongoing relationships among the professionals involved. The situation can be further complicated when there are a number of teams involved seeking multiple organs from the same body (243).

The transplant coordinator's role in motivating the families of potential organ donors is critical. Studies have shown that when the situation presents itself, between 70 and 80 percent of families will consent to donation on behalf of their deceased relatives. But, as in the blood donation context, misunderstandings can confound the situation. A Gallup poll showed that willingness to donate one's own organs after death is linked to perceptions about the success of the procedure. Of the 49 percent who agreed that kidney transplantation would "extend a person's life substantially, " 60 percent were willing to donate; but of the 42 percent who were uncertain and believed that a transplant "might or might not extend that person's life, " only 36 percent were willing to donate (460). And in a further parallel to blood donor motivation, there are apparent cultural barriers to donation; for example, blacks are substantially less likely than whites to agree to donation.

Another group in need of education about transplantation possibilities are the physicians and nurses on the "front lines" in community hospitals or trauma centers. As one student of the procurement system put it: "The 'keys to the kingdom' are held, in organ procurement, by the nurses and neurosurgeons (sometimes neurologists) in nontransplant hospitals" (451). It is often complained that this is the weakest link in the system. Physicians and nurses are often understandably reticent about broaching the possibilities of organ donation with grief-stricken and vulnerable families.

There has been criticism of the current system's overreliance on single individuals as transplant coordinators. Critics of the practice describe the coordinator's role as inherently stressful because

of the simultaneous dual allegiance to the donor's family and to the recipient and transplant team. These stressful and conflicting functions are often undertaken on a 24-hour-a-day, on-call basis. Red Cross spokespersons have argued that their cadre of volunteer and professional staff, experienced in motivating blood donors, would be well suited to the task of coordinating procurement and counseling the families of prospective donors (376).

The Red Cross first embarked on pilot programs in St. Louis, MO, and St. Paul, MN. In Minnesota, the opportunity for some Red Cross blood bankers long interested in tissue preservation and storage to get involved in organ and tissue procurement came about when the transplant coordinator at the University of Minnesota left and the Red Cross agreed to fill the gap. A March 1984 survey conducted by the Red Cross of its 57 regions revealed 6 with at least one active program in organ or tissue banking (or definite plans to begin within 6 months).

Thirteen regions are actively planning or investigating the need for a number of specific services: seven in the area of public and professional education, seven in bone banking, three in cornea retrieval, and one in skin banking. Thirty-two regions expressed some interest but were still in the investigatory stages of contacting other agencies, hospitals, and professional groups to assess possible roles for the Red Cross. Finally, representatives of six regions stated they were not planning to become involved in organ or tissue banking in the foreseeable future (51).

Upon reviewing the pilot programs in the Midwest and the survey of its regional centers, the Red Cross Board of Governors in 1984 adopted a policy statement, pledging to:

1. Participate in a national effort to increase the supply of tissues and organs for transplantation through a program of public and professional education and counseling.
2. Develop and coordinate systems for tissue donor identification, retrieval, distribution, and use that are equitable and meet high professional standards.
3. Provide tissue services to meet community needs as is feasible and appropriate.
4. Assess the need for, and when appropriate, develop programs in support of organ donation services.

In April 1984, the American Association of Blood Banks (AABB) also adopted policies relating to organ transplantation. It was agreed that the "AABB will promote, among its members, histocompatibility testing, organ procurement, tissue banking and organ exchange among members and non-members. " The AABB also opposes the buying and selling of organs. In its policy statement, it also argued against any "operational" role for the Federal Government, instead urging it to increase public awareness about organ donation and encourage development of private sector organ procurement agencies. According to the AABB, the Federal Government should also explore mechanisms to pay the medical bills of transplant patients (27).

Supply and Demand

The number of brain-dead bodies available and suitable for the procurement of organs for transplantation is estimated by the Centers for Disease Control to be approximatel, 20,000 annually; yet only 2,000 are actually used as donors. In a recent 2-year period at the University of Pittsburgh, 71 candidates for liver transplantation died while awaiting transplants. Of the 58,000 patients who are maintained on dialysis under the federally funded End-Stage Renal Disease Program, there are 8,000 listed on formal recipient registries, awaiting compatible donors (52). The AMA's Council on Scientific Affairs estimates that up to half of those on dialysis maybe eligible for transplant (37).

An additional supply issue involves organ preservation. Organs, once removed, must be transplanted quickly; hearts within 8 hours, kidneys within 30 to 50 hours (depending on the method of preservation), and livers within 4 hours. The "wastage" rate is quite high for a number of organs; e.g., about 20 to 25 percent of kidneys procured annually are wasted (460). (This con-

trasts with a wastage rate for kidneys of about 5 percent in Western Europe, which some have attributed to better typing and crosshatching capabilities.)

Recently, attention has been focused on the propriety of buying and selling human organs as a way to alleviate shortages. Much of this controversy can be traced to a proposal by a Virginia physician to open a brokerage service which would pay living kidney donors in the United States and the Third World **(463).** The hue and cry that greeted this proposal was considerable. The experience with the risk of blood from paid, "skid row" donors in the late 1960s and early 1970s has been frequently cited as a reason to be wary of embarking on commercial ventures in transplantation (231). Others have expressed concerns, often raised in the blood donation context, that the impact of payment will be to make it less likely for people to donate voluntarily.

The Uniform Anatomical Gifts Act and related Federal and State laws and regulations have not addressed the question of whether financial reimbursement could be provided to an organ donor or the donor's estate for the organ itself (as opposed to compensation for lost wages or medical expenses associated with the donation procedure). A number of groups, including the National Association of Patients on Hemodialysis and Transplantation and the International Transplantation Society, have issued statements opposing commercialism in organ transplantation. The Executive Council of the American Society of Transplant Surgeons (which includes virtually all of the organ transplant surgeons in the country) went so far as to agree to expel any member participating in a transplant "under proprietary conditions. " A number of States have considered or adopted legislation to ban the buying and selling of organs. All of these statutes have explicitly excepted blood and blood components, because they are "self-replicating fluids" (374).

Increasing attention has been given to making the most use of each individual donor by procuring multiple organs from each body. Yet the 110 aforementioned procurement agencies are ostensibly funded by the Federal Government for the sole purpose of kidney procurement. As one commentator has observed (450):

> Legally speaking, however, they are "kidney" procurement agencies. With trivial exceptions, each is totally funded by the End-Stage Renal Disease Program, a program that only pays for kidney acquisition. In practice, however, they have already exceeded that limitation. Almost all organ procurement agencies routinely attempt to retrieve corneas and, frequently, skin and bone as well. The added costs of such efforts are minimal as the tissue-specific banks usually do the actual excision themselves. All the agency does is ask the permission of the family, make arrangements in the hospital, and contact the eye, skin, or bone bank. Government ignorance or benign neglect has simply allowed these organ procurement efforts to "piggy-back" on kidney procurement without cost.
>
> As the number of liver and heart transplants has increased in the last few years, "kidney" procurement agencies have taken responsibility for locating these organs as well. The transplant centers needing such organs have reimbursed the agencies for the additional costs. So long as the number of non-renal transplants is 2 *or 3* percent of the number of kidney transplants, there is little problem with this informal, ad hoc approach. But what will occur when the percent is 10 percent, or 30 percent, or even 60 percent!

Thus, one of the reasons why blood bankers have been interested in organ banking is the need to develop "full-service" organ banks.

There are also a number of tissues of use in transplantation which do not have to be maintained in a "living" state and which carry no risk of rejection because of immunological barriers. Some of these, such as nerves, arteries, dura, and fascia, have been collected and stored (either freeze-dried or frozen) by individual surgeons for later use. Other tissues such as bone and corneas have been collected and distributed by banks established for these specific purposes (491).

One commentator has suggested that blood banks aggressively explore possibilities in bone transplantation, by undertaking the initial step of

contacting medical and dental schools and societies (especially departments of neurosurgery and orthopedics) to find potential clients. Because of recent breakthroughs and new uses, there may be needs going unmet in the absence of an adequate SUPPIY (296).

Bone harvesting must take place within 24 hours of the time of death. It is recommended that procurement take place in a sterile environment, such as an operating suite or under a laminar-flow hood, so that there is no need to sterilize the material prior to transplantation. Although there are obvious logistical and cost considerations in the use of such facilities, it may also be preferable to retrieval in a funeral home or blood collection center because of "psychological concerns" (296).

Bones can be stored in a variety of forms and used in many ways. They can be freeze-dried and kept in a vacuum; stored in this way they have been kept for up to 15 years without any diminution in clinical quality. Bones can also be deep frozen below –80° C for future use. Transplants of freeze-dried bone can be used to treat fractures, to reconstruct limbs after surgical removal of tumors, and to fill in bone cysts after cervical spinal fusions. Freeze-dried, crushed cortical bone has been especially useful in periodontal therapy and in maxilofacial surgery (473).

There are a number of uses for human skin, which can be procured from dead bodies and stored in a frozen state. Transplanted skin is especially critical in the treatment of severely burned patients and can be used to cover open wounds to ward off infection and guard against loss of water, electrolytes, protein, and heat—usually as an interim measure until the patient's own skin can be transplanted in an autograft procedure.

As with the establishment of bone banks, it has been suggested that blood banks interested in diversifying into skin banking first contact local trauma centers, plastic and reconstructive surgeons, burn treatment centers, and geriatricians to gauge the need for banked skin. The donor pool and economies of scale are such that it has been suggested that large metropolitan or regional blood banks are best suited for this enterprise. It has been estimated that investment in the equipment necessary for cryopreservation and microbiological screening and staffing costs make it inefficient to operate a skin bank using less than 50 donors per year (which would involve screening approximately 2,500 potential donors) (151).

Compatibility

Many in the blood banking field have considerable experience in doing the kinds of tests necessary to ensure immunologic compatibility. The use of donor-specific blood components for therapeutic procedures has led to the establishment of registries of donors, organized not only by ABO/Rh blood groups, but also by HLA types.

The Red Cross markets an HLA tissue typing tray, and also maintains files of donors with rare blood characteristics or needs. The AABB maintains a similar file, and there also is a similar file on an international basis. Since 1.970, the American Association of Blood Banks has had a Committee on Organ Transplantation and Tissue Typing. Upon the recommendation of this Committee, the AABB recently established a Bone Marrow Transplantation Information Service, "designed to speed the flow of information between the various centers while insuring individual rights to privacy and avoiding the expense and encumbrance of maintaining a registry" (249). The AABB collects information about potential recipients provided by transplant centers, including the name of a staff contact person, a coded identifier for the recipient and the recipient's HLA type, ABO/Rh type, and relevant diagnostic information. This information is compiled and distributed at regular intervals.

According to the former chair of the AABB Committee on Organ Transplantation and Tissue Typing: "The 'matching' and subsequent considerations are carried on directly between the centers involved; the AABB is not a party to these, nor indeed, will it even know when such negotiations are going on." The AABB does, however, anticipate conducting retrospective evaluations to judge the success of the procedures (249).

Use of such registries has not only raised hopes about increased ease of matching, but also has occasioned concerns about confidentiality of donor records and the integrity of the consent process