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REPORT TO THE CONGRESS

BY THE COMPTROLLER GENERAL OF THE UNITED STATES

Hepatitis From Blood Transfusions: Evaluation Of Methods To Reduce The Problem

Department of Health, Education, and Welfare

This report examines ways to reduce the incidence of hepatitis from blood transfusions, including the Department of Health, Education, and Welfare's plan calling for the elimination of the practice of purchasing blood.

GAO identifies a number of difficulties with eliminating purchased blood and makes several other recommendations to alleviate the problem.

GAO recommends

- --adopting a national or regional registry of unacceptable blood donors,
- --testing all units of blood for hepatitis by the best test available, and
- --emphasizing research to determine the effect frozen blood has on hepatitis and to alleviate problems associated with frozen blood.

MWD-75-82

FEB. 13, 1976

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COMPTROLLER GENERAL OF THE UNITED STATES
WASHINGTON, D.C. 20548

B-164031(2)

To the President of the Senate and the
Speaker of the House of Representatives

This report describes actions that the Department of Health, Education, and Welfare can take to reduce the hepatitis risk associated with blood transfusions. The many persons who contract hepatitis after receiving blood transfusions, the large cost to the Nation's economy, and the widespread concern about the problem prompted our review.

We made our review pursuant to the Budget and Accounting Act, 1921 (31 U.S.C. 53), and the Accounting and Auditing Act of 1950 (31 U.S.C. 67).

We are sending copies of this report to the Director, Office of Management and Budget, and to the Secretary of Health, Education, and Welfare.

Elmer B. Staats

Comptroller General
of the United States

Contents

ABBREVIATIONS

CDC	Center for Disease Control
CEP	counter-electrophoresis
FDA	Food and Drug Administration
GAO	General Accounting Office
HBsAg	hepatitis B surface antigen

HEW	Department of Health, Education, and Welfare
NIH	National Institutes of Health
RIA	radioimmunoassay

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COMPTROLLER GENERAL'S REPORT TO THE CONGRESS

HEPATITIS FROM BLOOD TRANSFUSIONS: EVALUATION OF METHODS TO REDUCE THE PROBLEM Department of Health, Education, and Welfare

D I G E S T

Based upon statistical information derived in the early 1970's, it was estimated that hepatitis associated with blood transfusions cost the Nation several hundred million dollars in 1 year. (See p. 2.)

Generally, a patient receiving a blood transfusion has a greater chance of contracting hepatitis from the blood received if that blood was purchased rather than donated. The Department of Health, Education, and Welfare (HEW) proposes to alleviate the hepatitis problem by switching to an all-voluntary blood system.

However, certain paid donors--particularly some of those associated with hospital blood banks which obtain blood from well defined and controlled donor populations--are less likely to transmit hepatitis than certain volunteer donors. (See p. 6.) Eliminating all blood from paid donors should reduce the overall incidence of post-transfusion hepatitis but also

--will eliminate a significant amount of paid blood that, in certain cases, is safer than volunteer blood,

--will have no effect on high-risk volunteer blood, and

--could cause blood shortage problems. (See p. 6.)

GAO proposed that the Secretary of HEW apply controls to help purge the system of high-risk donors--volunteer as well as paid. HEW disagreed, stating that the proposals were not workable or cost-effective and that an all-voluntary blood supply system would best combat post-transfusion hepatitis.

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Having evaluated HEW's comments, GAO is making recommendations which it believes will improve the quality of blood used in transfusions.

GAO recommends that HEW (1) conduct research aimed at developing objective criteria and methods for measuring the quality of blood banking operations and (2) not call for eliminating blood from paid donors donating at banks which can show a valid record of supplying high-quality blood. (See p. 25.)

Most blood banks use donor registries to prevent unacceptable persons (such as those known to have caused hepatitis in the past) from donating or selling blood. However, because of deficiencies in the operation of these registries, blood continues to be accepted from such persons and used in transfusions. (See p. 26.)

GAO also recommends that the Secretary of HEW promote the establishment of a registry listing individuals unacceptable as blood donors and employ procedures to develop an effective registry system. HEW concurred with the intent of GAO's recommendations but cited certain problems to be overcome. (See p. 37.)

Since July 1, 1972, the Food and Drug Administration has required that blood collected by interstate blood banks be tested for indications that it could cause post-transfusion hepatitis. The available tests are 15- to 40-percent effective. (See p. 41.)

The Food and Drug Administration did not require interstate blood banks to use the best test. In addition, it did not require intrastate blood banks, which collect about 40 percent of the Nation's blood supply, to perform any test. (See p. 41.)

GAO recommends that the Secretary of HEW develop a procedure (1) requiring that all units of blood collected be tested for indications of hepatitis by the best test available and (2) designed to insure that, in the future, new and improved tests are put into effect as soon as practicable. (See p. 46.)

HEW agreed and, effective September 1975, required all units of blood to be tested by the best test available.

Some scientific evidence indicates that using frozen and washed blood might reduce post-transfusion hepatitis. The evidence, however, is inconclusive, and other advantages and disadvantages of frozen blood must be assessed. (See ch. 5.)

GAO recommends that the Secretary of HEW emphasize research to determine the effects of freezing and washing blood on post-transfusion hepatitis and to alleviate the problems associated with frozen blood. (See p. 55.) HEW agreed.

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CHAPTER 1

INTRODUCTION

Viral hepatitis is a major public health problem and a matter of great concern in public health agencies, clinics, and research laboratories throughout the country. The term "viral hepatitis" includes at least two diseases, one caused by hepatitis A virus--"hepatitis A"--and another caused by hepatitis B virus--"hepatitis B."

Hepatitis A and hepatitis B symptoms are nearly the same. Early symptoms include fever, weakness, loss of appetite, malaise, headache, and muscle pains. Smokers may experience a striking loss of taste for cigarettes. These symptoms are frequently followed by jaundice. In an advanced case of hepatitis, jaundice generally reaches a peak within 2 weeks and then gradually subsides, usually clearing within 6 weeks. Despite the similarities in symptoms, fatalities are unusual in hepatitis A cases but more common for hepatitis B cases. The primary cause of death is liver failure.

Two fairly consistent patterns of transmission have been observed for hepatitis A and hepatitis B. Hepatitis A appears to be most frequently carried in the feces of infected individuals. It is usually spread by direct contact or by contaminated drinking water or food. Children aged 5 to 15 are most often affected, but their cases are generally mild. Epidemics of hepatitis A have been traced to contaminated water and food, such as milk, sliced meats, salads, and bakery products. It can also be acquired by eating raw or undercooked clams and oysters contaminated with hepatitis A virus.

The infectious agent of hepatitis A is thought to be present in the circulating blood of an individual for only a short time before the onset of illness. During this period it can be transmitted through such means as the transfusion of blood or blood products from infected persons and the use of contaminated needles by drug users. Using a recently developed test for detecting hepatitis A, researchers at the National Institutes of Health (NIH), Department of Health, Education, and Welfare (HEW), have shown, however, that the transmission of hepatitis A through the transfusion of blood or blood products is very rare.

In contrast, most hepatitis B cases result from blood transfusions from infected persons or from the use of contaminated needles by drug users. In a small percentage of cases, hepatitis B is transmitted through the use of contaminated needles for tattooing or ear-piercing.

Hepatitis transmitted through the transfusion of blood or blood products obtained from infected persons is called post-transfusion hepatitis and can be either hepatitis A or hepatitis B. According to NIH officials, recent studies have shown that some post-transfusion hepatitis cases are being caused by an unidentified agent other than hepatitis A or B viruses.

IMPACT OF HEPATITIS

A study prepared by officials of HEW's Center for Disease Control (CDC) estimates that in 1970 the impact of hepatitis in the United States was as follows:

	Post-transfusion-associated hepatitis	Non-post-transfusion Hepatitis A	Non-post-transfusion Hepatitis B
Deaths	3,700	1,014	460
Cases	92,000	500,000	70,000
Economic impact (millions):			
Direct costs (diagnosis, treatment, and prevention)	$40.9	$109.1	$31.1
Productivity losses (note a)	210.2	181.0	78.9
Total economic impact	$251.1	$290.1	$110.0

a/ Represents productivity losses of persons in the labor force due to absence because of illness or premature death.

According to a CDC official, sufficient data is not available to prepare a similar study for a period after 1970.

We were unable to identify any other studies that dealt with the cost and number of cases and deaths for the entire hepatitis problem. HEW's office of the Assistant Secretary for Health has, however, prepared a study on post-transfusion hepatitis which made the following estimates for 1970:

Deaths	1,000
Cases	120,000
Economic impact (millions):	
Direct costs (hospitalization)	$25.2
Productivity losses (note a)	70.5
Total economic impact	[b]$95.7

[a]Represents productivity losses of persons in the labor force due to absence because of illness or premature death.
[b]Does not include physician charges, or intensive care for those who eventually die.

The estimates in the two studies differ greatly with respect to deaths caused by and economic cost of post-transfusion hepatitis. A CDC official believed his estimates properly reflected the hepatitis situation based on the data available. The study prepared by the Office of the Assistant Secretary for Health indicated that its estimates may be understated.

We reviewed the post-transfusion hepatitis problem and evaluated four methods for reducing it.

POST-TRANSFUSION HEPATITIS

Post-transfusion hepatitis is caused by transfusing a unit of blood collected from a donor carrying the disease in his blood--a hepatitis carrier. The unit of blood collected is usually a pint. The hepatitis carrier may think that he is perfectly healthy, may not know he has had the disease, and, on physical or laboratory examination, may show no evidence of being a carrier.

There is no specific treatment for curing post-transfusion hepatitis. Usual therapy consists mainly of complete or partial bed rest and a nutritious diet. Most doctors consider it essential that patients abstain from alcohol during and for a prolonged period after their illness.

No vaccine is available to prevent hepatitis B; however, NIH officials said they are attempting to develop one. They estimated that this vaccine will not be available for at least 3 to 5 years.

In 1965 NIH researchers discovered a blood abnormality, called hepatitis B surface antigen (HBsAg), which has been linked to hepatitis B. Studies have shown that two-thirds of the people transfused with blood collected from donors with HBsAg will contract hepatitis.

FEDERAL REGULATION OF BLOOD

Because there is no vaccine to prevent post-transfusion hepatitis, all possible precautions must be taken to prevent the spread of the disease through blood transfusions. The Secretary of HEW regulates blood and blood products through two statutes--(1) section 351 of the Public Health Service Act, as amended (42 U.S.C. 262), which requires blood and blood components or derivatives to be safe, pure, and potent, and (2) the Federal Food, Drug, and Cosmetic Act of 1938, as amended (21 U.S.C. 301), which requires that certain products, including blood and blood products, be safe and effective. Regulations promulgated under these acts are designed in part to prevent the collection and infusion of blood and blood products capable of transmitting hepatitis. The Secretary of HEW has delegated responsibility for regulating blood and blood products to the Food and Drug Administration (FDA).

Until April 3, 1973, only blood banks in the District of Columbia or shipping blood in interstate commerce were required to be federally inspected and licensed. However, regulations published on January 31, 1973, require that, effective April 3, 1973, all blood banks register with FDA and be subject to its inspection.

As of October 1974, about 5,500 blood banks were registered with FDA, of which only about 275 were licensed to ship their products interstate. During 1971, blood banks licensed to ship interstate collected 5,626,200 pints of blood, representing about 60 percent of all blood collected in the United States.

Regulations require FDA to inspect licensed blood banks at least every year and banks operating intrastate every 2 years. These inspections generally include evaluations of donor suitability, blood collection techniques, and laboratory procedures.

On July 1, 1972, FDA required that all licensed blood banks start testing each donation of human blood for the presence of HBsAg. Blood that tests positive for HBsAg cannot be transfused or used in manufacturing injectible products. HEW estimates, however, that, depending upon the test used, only 15 to 40 percent of the units of blood capable of transmitting hepatitis will be detected. In

September 1975, FDA required intrastate blood banks to test for HBsAg by the same testing techniques used by licensed blood banks. (See p. 41.)

REPORTING HEPATITIS

Data on the incidence of hepatitis A and hepatitis B is collected by CDC. Physicians report hepatitis cases to State health departments, which in turn report to CDC. CDC officials estimate that only about 10 percent of the cases are reported to them. Because reports on the incidence of hepatitis provide no detailed information on individual cases, a surveillance program was developed to obtain such data as age, sex, race, residence, exposure history, and occupation of the victim and date of onset of the disease for individual cases. For cases of post-transfusion hepatitis, data on the blood transfused is also requested. Although CDC requests surveillance reports for all hepatitis cases, it only received reports for about 35 percent of the cases reported during 1973.

CHAPTER 2

EFFECTS OF ELIMINATING PAID BLOOD

Many studies have compared the risk of transmitting hepatitis through blood collected from paid versus volunteer donors (paid blood versus volunteer blood). These studies have generally shown that the risk of post-transfusion hepatitis is much greater from commercial paid blood than from volunteer blood. Commercial blood banks are proprietary in ownership and not located in hospitals.

Because of the risk involved in transfusing commercial paid blood, a number of recent State and Federal actions have been taken to eliminate, or substantially reduce, the use of paid blood. These actions include (1) the enactment of legislation in Illinois and the introduction of many bills in the 93d and 94th Congresses to discourage the use of paid blood and (2) the establishment of an HEW goal to have an all-voluntary blood donation system.

Our review disclosed that, although blood from paid donors is generally more likely to transmit hepatitis than blood from volunteer donors, some groups of paid donors--particularly some of those associated with hospitals which obtain blood from well defined and controlled population groups--appear to present a lower risk than many volunteer groups.

In addition, hepatitis is generally recognized to be much more common in drug addicts than other population groups, and most authorities believe that addicts would sell their blood rather than donate it. However, responses obtained in our survey of 1,321 known drug addicts indicated that addicts in this group were more likely to donate than sell their blood.

Although eliminating all paid blood should reduce the overall post-transfusion hepatitis problem, such action (1) will also eliminate a considerable amount of paid blood that, in certain cases, is safer than volunteer blood, (2) could cause blood shortage problems, and (3) will have no effect on high-risk volunteer blood.

PRIOR STUDIES COMPARING HEPATITIS RATES OF VARIOUS DONOR POPULATIONS

A study supported by NIH's National Heart and Lung Institute and published in 1972 compared the post-transfusion hepatitis risk from paid and volunteer blood. The study included 4,984 cardiovascular surgery patients who received an

average of 7.7 units of blood at 14 university medical centers. Of these patients, 157 contracted post-transfusion hepatitis and 5 died of the disease.

Of these 4,984 patients, 2,090 received transfusions that were identified as coming from a specific category of donor. The following table shows the number of hepatitis cases reported by donor category.

Donor category	Average number of units transfused	Patients studied	Hepatitis cases Number	Hepatitis cases Percent
Volunteer--Red Cross	7.4	715	10	1.4
Volunteer--other	6.4	354	6	1.7
Paid--hospital	6.3	396	13	3.3
Paid--commercial blood bank	4.9	625	33	5.3

These statistics suggest that paid blood is more risky than volunteer blood. The following table shows the percentage of commercial blood used and hepatitis cases by location.

Location of medical center	Number of post-transfusion hepatitis cases per 100 patients	Percent of paid commercial blood
Lexington, Ky.	-	3
Rochester, Minn.	0.5	less than 1
Minneapolis, Minn.	.6	less than 1
Atlanta, Ga.	2.0	-
San Francisco, Calif.	2.1	-
Houston, Tex.	2.2	100
Baltimore, Md.	2.3	24
Boston, Mass.	2.3	-
Indianapolis, Ind.	2.6	36
Columbus, Ohio	3.1	-
Cleveland, Ohio	3.3	44
Denver, Colo.	4.7	less than 1
Chicago, Ill.	8.1	38
Los Angeles, Calif.	8.6	57
Overall average	2.8	21

The only center which used 100-percent commercial blood ranked 6th out of 14 in the incidence of post-transfusion hepatitis. This center had a lower hepatitis rate than two others that were 100-percent volunteer and another that used less than 1-percent commercial blood.

In addition, officials of the medical center in Rochester, Minnesota, stated in 1974 that, during the previous 10 years, over 250,000 units of blood had been transfused, of which 60 percent was collected by the medical center's blood bank from paid donors. This center had the second lowest rate of post-transfusion hepatitis cases per 100 patients during the period of the study--March 1966 through January 1970. The officials added that the paid blood is collected from 6,000 to 7,000 people, most of whom live within 50 miles of Rochester and respond to calls for donations within 24 hours after notification. The people average about three donations a year.

Another large-scale study, conducted by the American National Red Cross, looked at HBsAg testing results for April through December 1971 at all 59 Red Cross donor centers, which do not pay their donors. The following geographical breakdown was obtained:

	Number of units collected	Number of positive HBsAg reports	Reported incidence per 1,000
Puerto Rico	9,590	33	3.44
Southeast	436,045	802	1.84
Southwest	203,478	315	1.55
South central	55,341	75	1.36
Northeast	1,323,348	1,401	1.06
Northwest	114,978	95	0.83
North central	453,338	323	0.71
Total	2,596,118	3,044	1.17

The incidence of HBsAg positives per 1,000 ranged from 0.2 in Waterloo, Iowa, and 0.29 in St. Paul, Minnesota, to 3.10 in Savannah, Georgia, and 3.44 in Puerto Rico.

The highest rates in the United States were found in the Southeast; all six centers with rates over 2.5 per 1,000 were in this area. The lowest rates came from the northeast and the north central area, where all eight centers with rates lower than 0.5 per 1,000 were located.

Although the variance in rates among locations is great, the Red Cross study did not conclude that location was the only reason for the difference. Instead, the study indicated that both the geographical area and the socioeconomic structure of the donor population affected HBsAg rates.

EFFECTS OF STUDIES SHOWING PAID BLOOD'S HIGH RISK

In addition to the National Heart and Lung Institute study, we identified eight other studies that claim to show the higher risk of transmitting post-transfusion hepatitis with paid blood than volunteer blood. With the exception of the National Heart and Lung Institute study, the other studies dealt with commercial blood and not with other types of paid blood. For example, one study shows that when the Hines, Illinois, Veterans Administration hospital changed from a commercial base (92 percent paid donations) to a volunteer system (96 percent voluntary donations), post-transfusion hepatitis decreased from 20.8 to 7.7 percent.

These studies have caused considerable concern among those involved in blood banking and have resulted in several actions aimed at eliminating or substantially reducing the amount of paid blood used. These actions, discussed in greater detail below, include

--passage of "The Blood Labeling Act" in Illinois,

--establishment of Federal goals, including eliminating commercialism in acquiring whole blood and blood components for transfusion,

--introduction in the Congress of legislation designed to reduce or eliminate paid blood,

--adoption by the American Blood Commission of an all-voluntary blood system as a principal goal, and

--a proposal by FDA to label blood as paid or volunteer

The American Blood Commission is a nonprofit corporation established to implement the National Blood Policy announced by the Secretary of HEW in July 1973. (See p. 11.) According to HEW, the Commission's members represent collectors of more than 85 percent of the Nation's needed whole blood.

Effects of "The Blood Labeling Act" in Illinois

The Illinois law was designed to eliminate paid blood. HEW stated that, as a result of this law, reductions in the incidence of post-transfusion hepatitis are anticipated, but reliable data was not available to show such a reduction.

We learned that only the Chicago metropolitan area was affected by the law because it had historically been relying on paid blood whereas the remainder of the State had been using volunteer blood. Because the law only recently went into effect and because of the poor recording and reporting of post-transfusion hepatitis cases (see ch. 3), we were unable to determine the law's impact on the post-transfusion hepatitis problem. We were able, however, to obtain some information on its effects on the blood supply.

"The Blood Labeling Act," effective October 1, 1972, requires that (1) all blood be labeled as either purchased or volunteer and (2) after July 1, 1973, paid blood be administered only under the written direction of the treating physician and the reasons for its use be shown in the patients' medical records. Before the act over 50 percent of the blood transfused in Chicago was paid blood. Blood banks started shifting to volunteer donors at the first indication that the law would be passed. The amount of volunteer blood collected and transfused in Metropolitan Chicago has increased since the act was passed. At the completion of our fieldwork in March 1974, however, paid blood was still being collected and transfused in Chicago and volunteer blood was being shipped in from other States and from other areas of Illinois to meet the demand.

Although the law went into effect in October 1972, not until July 1, 1973, did the physicians have to show reasons for using paid blood. Most hospitals we visited have had to use some paid blood since July 1, 1973, because of emergencies. During 1973 one Chicago blood bank distributed 7,663 units of paid blood to Chicago area hospitals. A breakdown of paid blood distributed by this blood bank for the 6-month periods before and after July 1, 1973, is as follows:

	Paid units distributed
Before July 1, 1973	4,893
After July 1, 1973	2,770

Therefore, although paid blood continues to be used in Chicago, it is apparently used much less. In addition, during 1973 more blood has been shipped into the Chicago area than has been shipped out. During 1973 four major Chicago blood banks received 20,000 more units of blood from out of State than they shipped out of State. This represented about 15 percent of their available blood. In addition, one was shipping paid blood out of the State in return for volunteer blood. Chicago was also being subsidized by blood from other sections of Illinois. During 1973 a Peoria blood bank shipped over 4,000 units to the Chicago area.

Most blood bank officials believed that a completely volunteer system could work but would take time to become fully established. According to one blood bank official, Chicago was probably meeting its own population's needs with volunteer blood but a shortage is caused by many patients in need of major transfusions coming to Chicago from outlying areas.

Federal goals to eliminate paid blood

On July 10, 1973, the Secretary of HEW announced the National Blood Policy, which identified four goals for developing an improved blood service system.

1. Supply. A supply of blood and blood products adequate to meet all the Nation's treatment and diagnostic needs.

2. Quality. Attaining the highest standard of blood transfusion therapy by fully applying available scientific knowledge and by advancing the scientific base.

3. Accessibility. Access to the national supply of blood and blood products by everyone in need, regardless of economic status.

4. Efficiency. Efficient collection, processing, storage, and use of the national supply of blood and blood products.

To achieve these goals, the Policy called for attaining specific improvements in blood banking. Prominent among these is the transition to an all-voluntary blood donation system. The stated purpose of this change is to eliminate the acquisition of whole blood and blood components for transfusion from sectors of society in which transmissible hepatitis is particularly prevalent.

On September 24, 1973, the Secretary of HEW called on the existing organizations involved in providing blood services to undertake an intensive and concerted effort to produce a plan for implementing the National Blood Policy. These organizations included blood banking organizations, medical and hospital professional groups, health insurance organizations, and consumer groups.

In response to the Secretary's request, a proposal to establish an American Blood Commission was submitted to HEW on January 31, 1974. This proposal resulted from the efforts of the American Medical Association, American Association of

Blood Banks, Red Cross, Council of Community Blood Centers, American Hospital Association, American Society of Clinical Pathologists, and College of American Pathologists. On September 10, 1974, the Secretary indicated that the proposed plan was consistent with the National Blood Policy.

With respect to eliminating paid blood, the plan calls for a systematic and coordinated recruitment of volunteer donors. According to the plan, by the end of 1975 every blood bank associated with one of the three major blood banking organizations expected to be collecting all its blood from volunteer donors. These three organizations are the Red Cross; the American Association of Blood Banks, a nonprofit association for hospital and other blood banks; and the Council of Community Blood Centers, a nonprofit organization for blood banks. In 1971 these organizations collected about 80 percent of the Nation's blood supply.

The provisions of the plan approved by HEW do not apply to the collection of paid blood by commercial blood banks or the transfusion of paid blood by hospitals. Paid blood collected by a transfusing hospital is generally less likely to transmit hepatitis than paid commercial blood. (See pages 7 and 17.) Under the plan, paid blood will generally not be collected by the transfusing hospital. If this causes a shortage at the hospital, blood could be purchased from commercial blood banks.

Introduction of legislation in the Congress

During the 93d and 94th Congresses, at least 15 bills were introduced which were designed, in part, to reduce the incidence of post-transfusion hepatitis by discouraging the use of paid blood. A representative bill stated that:

> "* * * Congress further finds that * * * since the virus hepatitis, malaria, and other diseases are transmitted in human blood and are found significantly more often in the blood of persons who donate for monetary compensation than in the blood of voluntary donors, the purity and safety of the national blood supply is seriously threatened by the inadequate level of voluntary donation and by monetary compensation of blood donors. The Congress therefore finds that the welfare of the United States will be promoted by development of a 100 per centum voluntary blood supply as soon as feasible, that voluntary donation should therefore be encouraged and promoted, and that certain procedures and standards should be established with respect to the operation of all blood banks in the United States." (Underscoring supplied.)

Sponsors of two of these bills said that, although most blood banks have performed valuable services, some are relaxed in their efforts to screen donors and thereby collect contaminated blood. They indicated that this is particularly true of profitmaking (commercial) banks which purchase blood from donors such as alcoholics and drug addicts who sell their blood to support their habits.

FDA proposal to label blood

On November 14, 1975, FDA published in the Federal Register proposed regulations requiring blood to be labeled as paid or volunteer. In addition, the regulations would require that the label state that paid blood is associated with a higher risk of transmitting hepatitis than volunteer blood.

According to the proposal, FDA believes the requirement to so label blood (1) is necessary to provide physicians prescribing blood with important information regarding its source, (2) is consistent with the National Blood Policy objective to encourage, foster, and support efforts to establish an all-voluntary blood donation system, (3) will not interrupt blood services now provided, (4) will increase significantly the demand for blood from volunteer or paid donors from blood banks having evidence that their donor population is as safe as a volunteer donor population, and (5) will reduce the risk of transmitting hepatitis through transfusion. The proposal provided no guidance, however, as to what evidence is necessary to demonstrate that paid blood is as safe as volunteer blood.

Interested persons had until January 13, 1976, to submit written comments on the proposal.

IDENTIFICATION OF HIGH-RISK BLOOD DONOR GROUPS

To determine if the actions being taken to reduce or eliminate paid blood are justified, we developed HBsAg positive rates for 21 of the 31 blood banks included in our review. These 21 banks were selected primarily because (1) they were located in areas where both commercial and volunteer blood banks operated and (2) they collected substantial amounts of blood. The 21 blood banks collected blood at 32 locations. At 7 of the locations, blood was collected from both paid and volunteer donors, resulting in a total of 39 donor groups. Studies have shown that two-thirds of the people receiving transfusions with blood from donors testing HBsAg positive will contract hepatitis.

Although HBsAg positive rates are not a proven indicator of the infectivity of the donor population, studies have shown a correlation between such rates and actual cases of post-transfusion hepatitis. For example, the 1972 study of 14 medical centers (see p. 6) noted a high correlation between the HBsAg rate in the donor population and post-transfusion hepatitis. The study concluded that hepatitis varied, in order of correlation, with (1) the HBsAg rates, (2) the proportion of commercial donors, and (3) transfusion volume (i.e. the more blood a patient receives, the greater the risk of hepatitis). The conclusion about the correlation between HBsAg rates and actual cases of post-transfusion hepatitis was based on a random sample of blood donors at six of the medical centers.

For the blood banks reviewed, the overall HBsAg positive rate for paid blood was about three times higher than for volunteer blood. A breakdown of the 39 individual donor groups shows, however, that (1) some paid groups had a lower HBsAg positive rate than some volunteer groups and (2) paid blood collected by hospital blood banks had a lower overall positive rate than paid blood collected by commercial blood banks.

In addition, based on our analysis of 21 of the 39 donor groups, the HBsAg positive rates for these groups are apparently more directly related to the socioeconomic condition of the area from which they came than to whether they were paid or volunteer.

HBsAg rates for various paid and volunteer donor groups

We developed HBsAg positive rates for 39 blood donor groups (21 volunteer and 18 paid) in the Los Angeles, Chicago, and Baltimore areas and at the NIH Clinical Center, Bethesda, Maryland. These rates were generally based on 1972 blood collections.

The rates we developed are all based on the same test method for determining whether a donor's blood is HBsAg positive. According to HEW, this test--the counter-electrophoresis test--is 15-percent effective for detecting blood capable of transmitting hepatitis. Therefore, for every unit testing positive for HBsAg, there are about six other units not testing positive but capable of causing hepatitis. Chapter 4 contains information pertaining to the various tests used to detect HBsAg in blood.

For the period reviewed, the blood banks collected 118,553 units of blood from the 39 donor groups, of which

1,081 units tested positive for HBsAg. This represented an overall positive rate of 2.6 per 1,000. The following table shows the data for volunteer and paid donor groups.

	Number of donor groups	Units tested	Units positive	Positives per 1,000
Volunteer	21	300,860	506	1.7
Paid	18	117,693	575	4.9
Total	39	418,553	1,081	2.6

This analysis indicates that, overall, paid blood is about three times as likely to transmit hepatitis as volunteer blood. However, some paid groups had lower positive rates than some volunteer groups. The breakdown also shows that, of the eight donor groups with positive rates of less than 1 per 1,000, three are paid groups. Each area--Baltimore, Chicago, and Los Angeles--has some paid donor groups with a lower HBsAg rate than some volunteer donor groups.

Donor group	Paid or volunteer	Rate per 1,000	Donor group	Paid or volunteer	Rate per 1,000
A	V	-	U	P	2.1
B	V	-	V	P	2.2
C	P[a]	-	W	V	2.8
D	V	0.6	X	V	2.9
E	V	.8	Y	P	3.0
F	P	.8	Z	P	3.5
G	P	.8	AA	V	3.8
H	V	.9	BB	V	4.1
I	V	1.0	CC	P	4.3
J	P	1.3	DD	P	4.4
K	V	1.3	EE	P	4.4
L	V	1.3	FF	V	4.7
M	V	1.3	GG	P	4.8
N	P	1.4	HH	P	5.0
O	V	1.4	II	V	5.6
P	V	1.5	JJ	P	6.7
Q	V	1.5	KK	P	6.8
R	V	1.8	LL	P	9.0
S	V	1.8	MM	P	11.0
T	V	2.0			

[a]We classified the blood collected by this blood bank (the NIH Clinical Center) as paid blood because it paid donors $25 for every second unit. About 92 percent of its 1972 donors received monetary compensation.

HEW officials advised us that a valid comparison of HBsAg rates must consider the percentage of blood collected from first-time donors. They stated that, if a blood bank collected a large percentage of blood from first-time donors, its HBsAg rate would be higher than that of a blood bank that collected a large percentage of blood from repeat donors. This is because repeat donors would have been previously screened and those testing positive for HBsAg would have been eliminated from the donor population. HEW officials stated that, because the test only detects one out of seven bad units of blood, HBsAg positive rates are not a good indication of the safety of blood unless they are related to the percentage of first-time donors. The officials stated that there are more first-time donors in a volunteer system than in a paid system.

Although it is entirely possible that a volunteer system has more first-time donors than a paid system, resulting in a higher HBsAg positive rate, HEW officials had no information showing the extent of the difference or its effects. They agreed, however, that not all paid blood has a high risk of transmitting hepatitis.

Donor groups U and FF in the table represent paid and volunteer donors at the same blood bank. In February 1974, the blood bank discontinued collecting blood from paid donors to comply with the National Blood Policy. However, this bank's HBsAg positive rate for paid donors was only 2.1 per 1,000, while its rate for volunteer donors was 4.7 per 1,000. According to an official at the blood bank, efforts were being made to increase volunteer donations to make up for the loss of paid donors. He also said that the rate was lower for paid blood because this blood was collected from repeat donors that were hospital employees that had been tested for HBsAg with each donation.

Donor group C with HBsAg positive rate of 0 represents employees at the NIH Clinical Center who are paid for their blood. Despite its low rate, the Clinical Center discontinued paying donors on January 1, 1974, to comply with the National Blood Policy. During the 6 months after that date, the Clinical Center collected 2,1[illegible]5 units of blood compared to the 2,548 units collected during the same 6 months of 1973.

According to HEW, both the gain of donors following institution of a paid donor system at NIH and the relatively small loss of donors following cessation of this system were caused by many variables, including the adoption of a computerized donor retrieval system, variations in donor recruitment campaigns, and changes in the donor population due

to abolition of the military draft. HEW calculates the reduction in donors to be 14 percent and states that it began while payment was still in use. HEW added that the Clinical Center has not had trouble obtaining sufficient blood from voluntary donors to meet its needs despite published recruitment messages by NIH.

On September 9, 1975, however, the Clinical Center issued an appeal for blood donors. The appeal stated that (1) the amount of blood collected by the Center fell short of meeting its needs, (2) the number of active NIH blood donors was at an all-time low, and (3) without additional NIH donors, the employees blood assurance program might have to be curtailed.

Further analysis of the paid donor groups showed that the overall positive rate for paid blood collected by hospital blood banks was lower than the rate for paid blood collected by commercial blood banks.

	Number of donor groups	Units tested	Units positive	Positive per 1,000
Paid-hospital	7	26,509	71	2.7
Paid-other (note a)	11	91,184	504	5.5
Total	18	117,693	575	4.9

[a]Represents commercial and nonprofit blood banks that pay their donors.

This data indicates that, overall, paid blood collected by hospital blood banks is about twice as safe as that collected on a paid basis by other blood banks in our sample. A breakdown by individual donor group indicates, however, that not all hospital paid donor groups are safer than other paid donor groups.

For example, of the 18 paid donor groups, a hospital blood bank had the second highest positive rate. In addition, of the four paid donor groups with the lowest rates, only two were hospital groups.

If the hospital with the highest positive rate was omitted from the above analysis, the average positive rate for the remaining six hospital blood banks that pay their donors is 1.7, which is comparable to the positive rate for volunteer blood banks. The hospital blood bank with the highest rate was the only one of the seven which did not screen donors for drug addiction.

HBsAg rates for various socioeconomic donor groups

Our review indicated that, although the overall HBsAg positive rate for paid donor groups was about three times higher than for volunteer donor groups, some paid groups had lower positive rates than some volunteer groups. (See p. 15.) For example, paid donors at one blood bank had a positive rate of 0 per 1,000, while volunteers at another blood bank had a rate of 5.6 per 1,000. To attempt to explain this variation, we looked for a possible association between the HBsAg rates and the socioeconomic condition of the area from which the blood bank drew its donors. A Red Cross study (see p. 8) had indicated that this factor affected the HBsAg rates.

We asked blood bank officials for precise geographical areas from which their donors were drawn. We selected 21 donor groups for which blood bank officials had knowledge about where their donors lived and for which blood screening techniques were approximately the same. We eliminated from our analysis blood banks that were collecting blood from a specific segment of the population, such as students or military personnel.

Using the geographical boundaries given by blood bank officials, we developed socioeconomic information, including income and housing characteristics, for these areas on the basis of 1970 census data. The table on the following page summarizes this information, indicating whether each group was a paid or volunteer group.

Although the average HBsAg positive rate was only 1.5 per 1,000 for the volunteer groups as opposed to 5.0 per 1,000 for the paid groups, our statistical analysis of the data shows that the socioeconomic conditions of the area from which the donors came was more strongly related to the HBsAg positive rates than was the factor of whether they volunteered or were paid. For example, the percentage of families below the poverty level, the factor with the highest degree of association with the HBsAg rate, statistically explains 63 percent of the differences among the blood banks' HBsAg rates. Whether the donors volunteered or were paid statistically explains 36 percent of the variation in the HBsAg rates. A more detailed explanation of our analysis is set forth in appendix IV.

Donor groups	Type of donor	HBsAg positives per 1,000	Income characteristics: Percentage below poverty level	Income characteristics: Estimated median family income	Housing Characteristics: Percent lacking complete plumbing	Housing Characteristics: Percent lacking complete kitchen	Housing Characteristics: Percent built before 1940
A	Volunteer	0.0	10.9	$ 4,371	1.2	1.1	18.0
D	Volunteer	.6	5.6	11,915	.6	1.0	7.5
E	Volunteer	.8	11.9	7,730	8.1	5.9	79.1
F	Paid	.8	4.8	7,735	2.2	.5	10.5
H	Volunteer	.9	3.9	11,075	1.5	.5	22.3
K	Volunteer	1.3	2.8	13,831	1.1	.8	17.9
L	Volunteer	1.3	2.8	13,831	1.1	.8	17.9
N	Paid	1.4	8.2	10,282	1.5	1.6	31.6
0	Volunteer	1.4	8.2	10,282	1.5	1.6	31.6
X	Volunteer	2.9	2.2	13,627	1.7	.7	13.5
Y	Paid	3.0	13.0	7,542	2.2	2.6	47.6
Z	Paid	3.5	9.9	10,535	1.9	3.2	32.2
CC	Paid	4.3	11.9	7,730	8.1	5.9	79.1
DD	Paid	4.4	15.4	8,642	5.0	3.2	66.1
EE	Paid	4.4	13.8	8,676	2.3	1.3	68.0
FF	Volunteer	4.7	26.2	6,843	3.2	3.7	82.4
HH	Paid	5.0	20.6	7,500	2.8	3.3	79.3
JJ	Paid	6.7	38.2	3,747	34.3	47.7	81.7
KK	Paid	6.8	13.0	7,542	2.2	2.6	47.6
LL	Paid	9.0	17.5	8,251	6.5	5.3	75.5
MM	Paid	11.0	38.2	3,747	34.3	47.7	81.7

The following table further demonstrates the positive relationship between higher HBsAg rates and the percentage of persons below poverty level in the area from which the donors were drawn.

Percent below poverty level of the drawing areas	Average number of positives per 1,000 donors
0 to 5	1.30
5 to 10	2.43
10 to 15	4.54
15 to 20	6.28
20 and above	7.73

Although the poverty-level factor seems to have a stronger association with high HBsAg rates than does the paid-volunteer factor, there are exceptions. For example, two donor groups with positive rates of less than 1 per 1,000 have a percentage below poverty level of more than 10. In contrast, six of the donor groups with positive rates in excess of 1 per 1,000 have a percentage below poverty level of less than 10.

DONATIONS BY DRUG ADDICTS

Various studies indicate that the high incidence of post-transfusion hepatitis from paid blood is partly caused by commercial or profitmaking blood banks' obtaining blood from drug addicts, who have a very high rate of HBsAg positive blood. A study partly supported by the NIH grant funds shows that addicts' HBsAg positive rate is 42 times greater than that of the general population. We discussed this matter with officials of drug treatment centers, who believed that most addicts would not sell or donate their blood because

--they would expose themselves to possible identification and police harrassment,

--the money received for a unit of blood is small ($5 to $10) and does not go far toward supporting a habit, and

--addicts dislike letting anyone puncture veins they need to maintain their habit.

We distributed questionnaires (a copy of which is included as app. V) to various drug treatment centers in Boston, Baltimore, New York, Los Angeles, and Chicago. We requested that information from persons being treated be obtained through interviews conducted by center personnel. Many of 1,321 addicts interviewed that injected drugs responded that

they sold or donated their blood. The addicts indicated that these donations and sales took place after they had become addicted to drugs. The following table is a summary of the questionnaire responses.

	Total	Boston	Baltimore	New York	Los Angeles	Chicago
Number of responses	1321	305	212	464	166	[a]174
Donations by addicts:						
Number who reported attempts to donate	199	63	24	38	53	21
Number who reported donations	165	60	13	27	47	18
Units reported donated	777	322	31	45	328	51
Units reported donated after having hepatitis	114	76	2	6	28	2
Sales by addicts:						
Number who reported attempts to sell	140	19	21	15	63	22
Number who reported sales	129	18	16	14	60	21
Units reported sold	756	182	33	69	357	115
Units reported sold after having hepatitis	129	2	5	16	74	32
Overall (donate and/or sell)						
Number who reported attempts to donate and/or sell	[b]287	82	39	47	83	36
Number who reported donations and/or sales	[c]252	78	26	36	79	33
Units reported sold or donated	1533	504	64	114	685	166
Units reported sold or donated after having hepatitis	243	78	7	22	102	34

[a]An undetermined number of these questionnaires were completed by the addicts rather than through interviews with drug center personnel.
[b]Includes 52 addicts who indicated that they have attempted to donate and sell their blood.
[c]Includes 42 addicts who indicated that they have donated and sold their blood.

Federal regulations for interstate blood banks state that no individual shall be used as a source of blood for transfusion if he has

--a history of viral hepatitis or

--skin punctures or scars on his arms or forearms indicative of addiction to self-injected narcotics.

This data, however, indicates that drug addicts have been successful at donating and selling their blood. Of 287 addicts who reported attempting to donate or sell their blood, 252 (88 percent) reported they were successful. They reported donations and sales of a total of 1,533 units of blood, 243 after they knew they had hepatitis. Other addicts may have had hepatitis without knowing it.

HEW COMMENTS AND OUR EVALUATION

In bringing our findings to HEW's attention, we proposed that it:

--Establish, for blood banks, maximum acceptable incidence rates of (1) positive findings of HBsAg and (2) actual diagnosed cases of post-transfusion hepatitis resulting from the transfusion of blood collected by particular blood banks.

--Periodically review the HBsAg positive rates of blood banks and the cases of post-transfusion hepatitis resulting from the transfusion of blood collected by the banks to insure that they are within the established limits. The extent and priority in scheduling these reviews should be determined on the basis of factors which show a high correlation with post-transfusion hepatitis, such as the percentage of persons below property level in the donor's neighborhood and whether the donor is paid or a volunteer.

--Delete from the National Blood Policy the provision calling for eliminating the practice of purchasing blood from donors and, in its place, require each blood bank to stay within the limits described above.

--Make known to blood banks our findings about drug addicts donating and selling their blood and stress the importance of not accepting them as donors.

Except for the last proposal (with which it agreed with some reservation), HEW strongly disagreed with our proposals. (See app. I.) It pointed out many problems it perceived as bearing on the feasibility and practicality of the first two proposals. Concerning the third, it believed that more could be done to prevent transfusion-related hepatitis by relying totally on unpaid donors than by any other single measure or combination of measures.

Comments received from the American Blood Commission were in general consonance with those of HEW. (See app. III.)

Although we do not agree with all the reasons HEW gave for opposing our proposals (See app. II for our detailed analysis of HEW's comments on these proposals), we have concluded that establishing, as bases for direct blood bank regulation, (1) specific maximum rates for positive findings of HBsAg would not be feasible and (2) specific acceptable incidence rates for post-transfusion hepatitis would, given the problems in obtaining valid data on such cases (see ch. 3), be at best questionably practical at the present time.

We continue to believe, however, that these indicators, and the others mentioned in the second proposal, can be useful bases for (1) establishing priorities for and the frequency of inspections of blood banks and (2) offering suggestions for changes in practices to improve blood quality.

Regarding the third proposal, we agree that switching to an all-voluntary blood supply, if it can be accomplished without causing shortages, would be expected to reduce the overall incidence of post-transfusion hepatitis.

Evidence clearly indicates, however, and HEW agrees, that some blood banks which pay their donors supply blood of relatively high quality and of a higher quality than others which rely fully on volunteer donors. This is particularly true of hospital-operated blood banks which obtain blood from well defined and controlled populations. We believe that the part of the National Blood Policy which calls for moving toward an all-voluntary system should not arbitrarily call for eliminating paid blood from banks which can show a valid record of supplying high-quality blood, particularly if such action could jeopardize the adequacy of the blood supply or force a reliance on blood from other sources, from either paid or volunteer donors, which is or may be of lesser quality.

Additionally, merely moving to an all-voluntary blood supply will clearly have no effect on the incidence of hepatitis caused by volunteer blood collected by banks which do not have a record of supplying high-quality blood. Although the measures suggested in chapters 3 and 4 (with which HEW generally agrees) should result in some improvement in this regard, we believe that HEW should consider conducting research aimed at developing objective criteria and a methodology for measuring the quality of blood banking operations to be used in directly regulating blood banks. Such research should include a study of the feasibility of using actual hepatitis rates as a measure of blood banks' operations.

RECOMMENDATIONS TO THE SECRETARY OF HEW

We recommend that the Secretary:

--Conduct research aimed at developing objective criteria and a methodology for measuring the quality of blood banking operations for use in directly regulating blood banks.

--Use indicators--such as HBsAg positive rates, incidence rates of post-transfusion hepatitis, percentage of persons below the poverty level in the donor's neighborhood, and whether the donor is paid or a volunteer--as a basis for establishing priorities for and frequency of inspections of blood banks and for suggesting changes to improve blood quality.

--Modify the National Blood Policy so that it does not call for eliminating paid blood from banks which can show a valid record of supplying high-quality blood.

--Make known to blood banks our findings about drug addicts donating and selling their blood and stress the importance of not accepting them as donors.

CHAPTER 3

DEVELOPING A FEDERAL REGISTRY OF UNACCEPTABLE DONORS

Blood banks generally maintain a registry to identify donors that are carriers of hepatitis to prevent the future collection of their blood. Information used by the blood banks to identify hepatitis carriers includes (1) the results of screening of donors by the blood banks for such things as signs of drug addiction, (2) the results of HBsAg testing, (3) reports from other blood banks on donors that are carriers, and (4) reports from hospitals on cases of post-transfusion hepatitis that resulted from the use of blood furnished by the blood bank.

No uniform criteria existed for determining whether a donor should be classified as unacceptable; blood banks were unaware of many post-transfusion hepatitis cases that resulted from the use of their blood; information on unacceptable donors was generally not exchanged between blood banks; blood banks often did not properly maintain their registries; and some blood banks did not even use a registry. Therefore, attempts to prevent hepatitis carriers from donating blood by using registries have often proven ineffective.

We believe there is a need for (1) criteria for determining whether an individual is unacceptable and (2) a registry of donors that are determined to be unacceptable under those criteria. The system for obtaining much of the information needed for such a registry exists, but the information is incomplete and is used for other purposes. We believe that, with some additional cost and with strong enforcement, a system could be developed which would greatly reduce the post-transfusion hepatitis problem.

SYSTEM FOR REPORTING HEPATITIS CASES

The National Morbidity Reporting and Surveillance of Communicable Diseases system is a cooperative system between CDC and the various State health departments. The State health departments report the incidence of about 30 communicable diseases, including hepatitis A and hepatitis B, to CDC weekly. CDC officials estimate, on the basis of past studies, that only about 10 percent of the actual cases are reported to them. CDC gathers additional, more detailed information from the State health departments on 12 of the diseases, including hepatitis. For cases of post-transfusion hepatitis, this includes the name of the patient and hospital where the transfusion was performed.

Although CDC requests the additional data for all hepatitis cases, it receives such data for only about 35 percent of the cases initially reported by the States. The additional information is reported on a Viral Hepatitis Case Record. CDC uses all the data for monitoring current trends.

Reporting post-transfusion hepatitis cases to CDC

State laws governing the three areas in which we reviewed the reporting of hepatitis cases--Boston, Chicago, and Los Angeles--require doctors and hospitals to report hepatitis cases to the State or local health departments. Reports made to local health departments are forwarded to the State health departments, which, in turn, send them to CDC.

Only a small percentage of the diagnosed and hospitalized cases of post-transfusion hepatitis were being reported to the State or local health departments. Therefore, the number of cases being reported to CDC by the State health departments do not show the magnitude of the problem.

For example, the records of two blood banks in Chicago showed that hospitals had advised the blood banks that 172 cases of post-transfusion hepatitis had resulted during fiscal years 1972 and 1973 from blood furnished by them. The hospitals reported only 30 of these cases to the local health department.

In addition, health departments in Illinois received reports for only 131 cases of post-transfusion hepatitis for the entire State during fiscal years 1972 and 1973. All the cases were reported by hospitals and none by private physicians. CDC and the Office of the Assistant Secretary for Health both estimate that about 50 percent of known cases of post-transfusion hepatitis are treated by private physicians and do not require hospitalization.

A Chicago Board of Health study covering September 1, 1972, through August 31, 1973, showed that, of 74 cases of post-transfusion hepatitis diagnosed by Chicago hospitals, only 6 (8 percent) were reported to the board of health.

A similar California Department of Health study showed that 200 sampled hospitals reported only 32 cases of hepatitis B in 1971, whereas the hospitals' medical records showed a total of 174 cases. For 27 hospitals reviewed in Los Angeles County, only 11 of 63 cases (17 percent) were reported.

At four Boston area hospitals we identified 19 cases of post-transfusion hepatitis that had been diagnosed during fiscal years 1972 and 1973 and should have been reported to the State health department. State health department records indicated that the hospitals reported only eight (23 percent) of the cases.

Although some State laws require reporting post-transfusion hepatitis cases, many cases are apparently not being reported. According to health department officials from these three areas, no legal action has been taken to penalize those who neglect to report. Of the three States, one had no penalty for failure to report cases of post-transfusion hepatitis, another provided only for a fine, and the third provided for a fine and/or jail sentence.

NO UNIFORM CRITERIA FOR EXCLUDING DONORS

For a Federal registry of unacceptable donors to be feasible, there must be uniform criteria that the blood banks could use for including an individual's name on the registry.

We obtained the criteria used by 16 blood banks in Baltimore, Boston, Chicago, and Los Angeles to classify a donor as unacceptable and found that diverse criteria were being used, as shown in the table on the following page.

Thus, two blood banks would not reject a donor even if his blood had been the only blood used in a previous transfusion and the patient was stricken with post-transfusion hepatitis, whereas another blood bank rejected all donors implicated in a case of post-transfusion hepatitis, regardless of the number of other donors involved. This diversity of criteria makes exchanging information between blood banks difficult, because donors that are unacceptable to one may be acceptable to another.

Criteria	Number of blood banks using criteria to reject donors
Donor's blood tested positive for HBsAg	16
Medical history of hepatitis or jaundice	16
History of drug abuse	14
Donor associated with one post-transfusion hepatitis case and the donor's was the only blood used	14
Donor associate' with two post-transfusion hepatitis cases in which patients received more than one unit of blood	12
Donor's blood showed yellow serum indicating a liver function problem	3
Donor associated with one post-transfusion hepatitis case where patient received more than one unit of blood and tests showed abnormal liver functions	3
Donor associated with one post-transfusion hepatitis case and this was his first donation	2
Donor implicated with a case of post-transfusion hepatitis when recipient got five units of blood or less	2
Donor associated with one post-transfusion hepatitis case	1
Donor associated with one post-transfusion hepatitis case involving two units of blood or number of units of blood unknown	1

FDA regulations for licensed blood banks and proposed regulations for registered blood banks state that no individual shall be used as a source of blood for transfusion if he has

--a history of viral hepatitis,

--a history of close contact with an individual having viral hepatitis within 6 months of donation,

--skin punctures or scars on his arms indicative of addiction to self-injected narcotics, or

--tested positive, or is known to have tested positive in the past, for HBsAg.

These regulations do not provide for rejecting donors who have been implicated in one or more cases of post-transfusion hepatitis.

In addition to the FDA regulations, the American Association of Blood Banks recommends to its member banks that a donor be permanently excluded if (1) his was the only unit of blood, blood component, or derivative administered to a patient who developed post-transfusion hepatitis within 6 months or (2) more than one recipient receiving blood, blood components, or derivatives prepared from his blood have developed post-transfusion hepatitis.

The Association standards also recommend that, if a donor is not excluded on the basis of his implication in a case of post-transfusion hepatitis in which the patient received blood from more than one donor, the case should be reviewed by the blood bank's physician.

The Red Cross requires its centers to follow all the above criteria set forth by FDA regulations and the association.

BLOOD BANKS UNAWARE OF POST-TRANSFUSION HEPATITIS CASES

For cases of post-transfusion hepatitis, the local health departments in Chicago and Los Angeles obtain from the hospitals in their area the identifying numbers of the units of blood transfused and the names of the blood banks supplying the blood. According to the local health departments, they do not forward this information to the blood banks.

Hospital and blood bank officials in these areas said they have an informal system for identifying hepatitis carriers whereby the hospitals notify the blood banks of any units of their blood involved in a case of post-transfusion hepatitis. The blood banks, in turn, note this information in the donor records.

In the Boston area the State health department notifies the Massachusetts Red Cross Blood Program of cases of hepatitis reported by hospitals. The Red Cross then notifies the hospital performing the transfusion and requests identifying information for any Red Cross units transfused.

The identifying information is used by the Red Cross to note on donor records that the donors were implicated in a case of post-transfusion hepatitis. This may cause the donor to be excluded from making future donations.

To determine the effectiveness of the informal reporting systems used in the Los Angeles and Chicago areas, we selected 1,493 units of blood which hospitals reported to the local health departments as being involved with post-transfusion hepatitis cases during fiscal years 1972 and 1973. Also, from our review of records at four Boston area hospitals, we selected 231 units of blood which the hospitals identified as being involved with post-transfusion hepatitis cases during the same period We selected these 1,724 units because they were collected by 13 blood banks we had selected for review, 8 in the Chicago area, 3 in the Los Angeles area, and 2 in the Boston area. All 13 blood banks maintained a registry of unacceptable donors.

In 748 cases the blood banks did not note on the donor records that the donor's blood was involved in this case of post-transfusion hepatitis.

	Units involved	Donor records not noted	
		Number	Percent
Chicago	955	174	18
Los Angeles	538	425	79
Boston	231	149	65
Total	1,724	748	43

The schedule shows that, in 43 percent of the cases reviewed, the blood banks were either not notified of the unit's involvement with post-transfusion hepatitis or did not record the information in their records.

According to the blood banks' criteria, 78 of the 748 donors would have been placed on the blood banks' registries of unacceptable donors if the banks had been made aware of and had recorded the donors' involvement with cases of post-transfusion hepatitis. This would have prevented the 78 donors from making future donations at these blood banks.

LACK OF INFORMATION EXCHANGE BETWEEN BLOOD BANKS

Most of the blood banks we reviewed maintained some type of records on permanently rejected donors, but the areas we reviewed had no central registries listing all rejected donors. The exchange of donor information between blood banks was poor, resulting in many persons being accepted as donors at one blood bank after being classified as hepatitis risks by another. This problem would not exist if donors consistently attempted to give blood at the same blood bank or if blood banks exchanged donor information.

We reviewed donor mobility in the Chicago, Los Angeles, and Baltimore areas and noted many instances in which donors had given blood at more than one blood bank. According to a blood bank official, this is due to natural moving habits and the desire to donate at the most convenient location. Also, with the trend toward industrial and community blood donations, a person could donate at work and in his community. In addition, replacement donors tend to donate at the patient's hospital, no matter where they live.

The Red Cross maintains a national registry of unacceptable blood donors, which is used by its 59 centers to identify unacceptable donors. During our review, however, the information was not generally exchanged with other blood banks near the centers. Since the inception of its national donor registry in 1971, the Red Cross' policy has been to encourage the exchange of information with other organizations. In January 1975, however, the Red Cross said that only 13 organizations had agreed to exchange information with it on unacceptable donors.

Chicago area

The Chicago Board of Health requires every blood bank in the city to submit information, including the donor's name, address, birth date, social security number, and blood type, on all donors who test positive for HBsAg. The board of health sends a monthly report listing each such donor to blood banks within the city. However, only four of the eight blood banks in Chicago that we visited used the listings. The four blood banks not using the listings

did not do so because (1) one did not receive the listings, (2) two would not rely on other blood banks' information, and (3) the fourth could not afford the time to check donors against the lists.

The Chicago Board of Health does not attempt to collect information on persons permanently rejected by blood banks for reasons other than positive HBsAg test results. The blood banks in the area do not usually exchange any type of information.

Our review of donors reported by the board of health and to blood banks in the Chicago area showed that between March 1970 and January 1974, 1,128 donors had been reported as testing positive for HBsAg. FDA regulations state that, if a person's blood is found to test positive for HBsAg, a blood bank may not use his blood for transfusion purposes.

We also found that 65 of these donors (55 paid donors and 10 volunteer donors) were tested as being positive for HBsAg at more than one blood bank. Eighteen of these were tested positive at three or more locations.

The fact of donor mobility and the need for exchange of information among blood banks are further demonstrated by our review of donor records at two blood banks. We found that 48 donors were rejected and placed on the registry of unacceptable donors at one blood bank because they had been involved with cases of post-transfusion hepatitis. Of these, 11 subsequently donated blood at the second bank.

Los Angeles area

Three Los Angeles-area commercial blood banks, operating a total of five donor collection centers, were included in our review. Officials of these banks believed that many persons donate blood at more than one location and consequently had established a system for the banks to report weekly to each other the names of rejected donors. This was the only information exchange we noted between Los Angeles-area blood banks.

To determine these donors' mobility and this system's effectiveness, we analyzed th records for about 1,700 individuals whose last names begin with the letter R and who had donated blood at four of the five donor collection centers (three in Los Angeles and one in Long Beach) during the year ended June 30, 1973.

Of the 1,700 individuals, 195 (about 11 percent) had donated at more than one of these centers. Also, 33 had

donated in both Long Beach and Los Angeles, which are about 25 miles apart.

Of the 1,700, 237 were classified as unacceptable donors and therefore should have been excluded from donating at all four centers. Of the 237, 16 were subsequently accepted as donors at one of the other centers. They donated 27 units of blood after they had been classified as unacceptable. Officials at these blood banks believed that this had occurred because the donors' names were not reported into the system or the information was not conspicuously annotated on all donor records. We were not able to determine the number of unacceptable donors rejected as a result of this system because records were not maintained for such rejections.

Baltimore area

In the Baltimore area, we compared donor records at two blood banks to determine if (1) the same donors were donating at both banks and (2) the banks had information that should be shared.

We cross-checked about 1,400 names and found that 31 had donated or attempted to donate at both blood banks. Two of these donors had been rejected by one blood bank and had subsequently donated a total of five units at the other blood bank. If these banks had shared donor information, the second bank would have known not to accept these donors.

IMPROVEMENTS NEEDED IN DONOR REGISTRIES

There were many instances in which the maintenance of donor registries in all four cities visited could have been better.

Boston area

At one blood bank, a registry of undesirable donors was maintained but used only to avoid calling such donors to solicit blood. It was not used for its primary purpose--screening walk-in donors.

The blood bank generally relied instead on HBsAg testing and donor notification letters to prevent unwanted donations. As previously noted, however, HBsAg testing only detects 15 to 40 percent of the units of blood capable of transmitting hepatitis. Moreover, 9 of the 16 donors rejected during fiscal years 1972 and 1973 because of positive HBsAg test results were not advised against further donations. As a

result of these deficiencies, one donor has been implicated in three post-transfusion hepatitis cases.

After discussions with us, officials of the blood bank established a donor registry in their donor room and now screen all prospective donors. As a result, at least one donor has been classified as unacceptable who had previously been implicated in two cases of post-transfusion hepatitis and had been notified not to donate again.

Officials at another blood bank said they maintained a listing of unacceptable donors, but they were unable to locate it at the time of our review. We attempted to review the records for 11 donors implicated in post-transfusion hepatitis cases. The records for five showed no indications that they were associated with post-transfusion hepatitis. We were unable to locate the records for the other six.

Chicago area

One blood bank collected about 95 percent of its donations by bloodmobiles. According to an official of this blood bank, the units collected are not checked against the registry of unacceptable donors until about 10 days after collection, by which time the blood may have already been transfused. If the donor had been previously rejected and the unit was already shipped to a hospital, the hospital would be notified to discard the unit. If the unit had been transfused, the patient's doctor would be notified.

Another blood bank's registry included only unacceptable donors who tested positive for HBsAg and not those rejected for such reasons as indications of drug addiction. Moreover, the registry was not being effectively used. Donors testing positive for HBsAg were notified by mail not to give blood again. Blood bank officials believe that this effectively precludes their returning to donate. Records show, however, that three positive donors each gave a unit of blood in 1973 after being notified not to donate again. Fortunately, their blood again tested positive and was discarded.

Los Angeles area

At one blood bank, we traced to the donor records 19 units of blood that had tested positive for HBsAg. The records of 11 had not been properly annotated. As a result, two of these donors made subsequent donations, which tested negative and were transfused. The blood bank manager attributed the failure to annotate the records to technician oversight or carelessness.

Another blood bank without a donor registry indicating unacceptable donors established one after our review.

CONCLUSIONS

Although hospitals and blood banks use various procedures to prevent unacceptable donors from donating blood, the procedures are, for the most part, ineffective. As a result, identifiable infected blood is being transfused because (1) no uniform criteria exist for classifying donors as unacceptable, (2) many cases of post-transfusion hepatitis known to hospitals are not reported to the blood banks, (3) information on unacceptable blood donors is generally not exchanged among blood banks, (4) blood banks often do not properly maintain their registries, and (5) some blood banks did not even use a registry.

We believe a registry should be established, either on a regional or national basis, listing individuals unacceptable as blood donors. The registry should include individuals (1) testing positive for HBsAg, (2) whose blood caused, or was suspected of causing, a case of post-transfusion hepatitis, or (3) with a history of viral hepatitis. Establishing a registry would require FDA to set forth additional criteria for classifying donors as unacceptable if their blood is implicated in one or more post-transfusion hepatitis cases.

In our opinion, the authority to establish such a registry exists under section 361 of the Public Health Service Act (42 U.S.C. 264), which provides that the Surgeon General can make regulations necessary to prevent the introduction, transmission, or spread of communicable diseases from one State to another. Section 361 mentions certain measures, such as inspections, pest extermination, and destruction of infected animals, that can be used to enforce the regulations. We believe establishing a registry is less drastic than measures mentioned in section 361 and that HEW can require the reporting of any information useful to prevent post-transfusion hepatitis.

To provide for effectively identifying hepatitis carriers, the CDC system for obtaining data on hepatitis cases should be strengthened and reporting of all post-transfusion cases of hepatitis made mandatory. Such a system could provide data for a registry of unacceptable donors, which could be used by blood banks to screen donors.

We proposed that the Secretary establish a Federal registry of unacceptable blood donors and periodically disseminate it to blood banks. To develop an effective registry system, HEW should

--require hospitals and doctors to report all post-transfusion hepatitis cases,

--standardize the criteria for classifying a donor as unacceptable,

--periodically review the blood banks' operations to insure that the registry is used effectively, and

--require blood banks to report all HBsAg positive test results.

HEW COMMENTS AND OUR EVALUATION

HEW disagreed with our proposal that the Secretary establish a Federal registry of unacceptable blood donors and periodically disseminate it to blood banks. HEW stated that the Privacy Act might require that all potential donors be informed of all uses made of the information gathered from them at the time of the blood donation. According to HEW, this might act as a deterrent to donors and could result in a serious reduction in blood collections.

HEW also stated that two blood banking experts--one on behalf of the Red Cross and one on behalf of another organization--have argued that it may not be cost-effective to check every potential donor against a national registry of disqualified persons. However, HEW advised us that, to explore the feasibility of donor registries, it is fostering, through the American Blood Commission, the development of mechanisms for sharing information regionally within the private sector. According to HEW, the Commission will be asked to consider each of our recommendations and take appropriate action in concert with FDA.

HEW also advised us that:

--Although the American Blood Commission will undoubtedly give high priority to uniform criteria for donor exclusion, establishing such criteria is difficult.

--Having hospitals and physicians report post-transfusion hepatitis cases and HBsAg positive test

results is desirable, but any reported cases must actually be confirmed as having the disease.

In our opinion, a regional donor registry system will achieve the purpose of our proposals if HEW monitors the system to insure that the deficiencies we noted in other donor registry systems do not also occur in this system. We do not believe, however, that cost is a significant problem in establishing a national registry. For example, the Red Cross, which collects an estimated 40 percent of the Nation's blood supply, maintains a national registry. According to a Red Cross official, the annual cost to maintain this system is between $338,500 and $363,500, exclusive of overhead. This includes the cost of maintaining the registry and of checking donors against the registry.

Considering that most blood banks reviewed maintained registries of unacceptable donors and considering the relatively minor cost of the Red Cross registry, cost would not appear to be a significant factor in determining the feasibility of a regional or national registry.

Regarding uniform criteria for excluding donors, the American Blood Commission advised us on June 23, 1975, that adequate criteria for screening donors with a history of hepatitis or positive tests for hepatitis and for any reason which might make them suspect are well established and accepted by all the blood banking agencies in the United States. They stated, however, that individual blood banks may not follow the criteria.

Thus, criteria for screening donors apparently already exist, but individual blood banks are not required to follow the criteria established by the blood banking agencies. (See p. 28.) We believe that uniform criteria for excluding donors strictly adhered to by blood banks are necessary for a donor registry to be useful. Otherwise, in reporting information for registry purposes, blood banks would be reporting data inconsistently and the registry's effectiveness would be diminished.

Regarding HEW's comment that reported cases of hepatitis must be confirmed, CDC maintains a hepatitis surveillance program as discussed on page 5. As a part of this program, CDC requests that surveillance reports be submitted for all cases of viral hepatitis. These reports contain such data as the results of HBsAg tests, information on blood transfusions received, and information on other possible causes of hepatitis. We believe that, were all cases reported under the CDC hepatitis surveillance program, the program, with little modification, could be used to provide the information

on cases of post-transfusion hepatitis. We do not believe that, however, a case of post-transfusion hepatitis that has been diagnosed and reported to CDC by a hospital or a doctor needs to be confirmed.

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Concerning this chapter, the American Blood Commission made some of the same comments as HEW. It also said that blood banks have criteria for classifying a donor as unacceptable which can be enforced by FDA. We found, however, that a diversity of criteria exists for classifying a donor as unacceptable. For example, criteria recommended by the American Association of Blood Banks and required by the Red Cross provide for rejecting donors implicated in one or more cases of post-transfusion hepatitis. These criteria are not part of FDA regulations.

For a registry to be effective, we believe that FDA must develop consistent criteria for all blood banks.

RECOMMENDATION TO THE SECRETARY OF HEW

We recommend that the Secretary promote the establishment of either a national or a regional registry of unacceptable blood donors--incorporating the proposals set forth on page 37--which could be used by blood banks to screen donors.

CHAPTER 4

USING BEST TEST FOR DETECTING UNSAFE BLOOD

HBsAg is a substance found in the blood that indicates the presence of hepatitis B virus in the body. Studies show that persons transfused with blood containing HBsAg will generally develop post-transfusion hepatitis.

Several tests are licensed by FDA for blood banks to detect HBsAg. The most widely used tests use counterelectrophoresis (CEP) and radioimmunoassay (RIA). According to an FDA official, these tests are used by most blood banks for detecting and eliminating units of blood capable of transmitting hepatitis B. A positive test result indicates the presence of the hepatitis B virus, but a negative test does not rule out its presence because current techniques are not sufficiently sensitive to detect low HBsAg levels. In addition, no test for HBsAg will ever completely eliminate the post-transfusion hepatitis problem because some cases appear to be the result of something other than the hepatitis B virus.

Although the RIA test can detect twice as many units of blood capable of transmitting hepatitis than the CEP test, FDA did not require the approximately 275 licensed blood banks (banks located in the District of Columbia or involved in interstate commerce) to use the RIA test to detect HBsAg. According to FDA officials, FDA did not require the more effective test partly because (1) of a possible lack of sufficient testing materials for all blood banks and (2) the test results in the rejection of some blood which does not contain hepatitis. (See pp. 43 to 45.)

In addition, FDA did not have regulations requiring HBsAg testing by the approximately 5,200 blood banks involved only in intrastate commerce. We believe that FDA should have required all blood banks to use the best test available for detecting HBsAg in donors' blood. In our opinion, this would have greatly reduced the number of post-transfusion hepatitis cases nationwide.

FEDERAL REQUIREMENTS FOR HBsAg TESTING

The presence of HBsAg in human blood was linked to hepatitis in 1965. The effectiveness of tests for the presence of HBsAg in the blood vary widely and are generally classified by researchers as belonging to one of three generations. First-generation tests, the least effective, are not generally used anymore.

CEP and RIA are classified as second- and third-generation tests, respectively. The CEP test was licensed by FDA in February 1971 and the RIA test in July 1972. According to HEW's Office of the Assistant Secretary for Health, the CEP method is optimally capable of detecting 25 percent of the units of blood which will transmit post-transfusion hepatitis but in actual practice is only 15-percent effective. The RIA test may optimally be able to detect up to 50 percent of the units capable of transmitting post-transfusion hepatitis but in actual practice is actually only 30- to 40-percent effective.

FDA did not require interstate blood banks to test for HBsAg until July 1, 1972. Shortly thereafter, FDA informed them that, to comply with the regulations, they must use a test method at least as sensitive as CEP and advised them to gain experience with the RIA method. Even though the RIA test is at least twice as effective as the CEP test, FDA had still not required its use as of February 1975.

Intrastate blood banks were not subject to the July 1972 testing requirements. On May 28, 1974, proposed regulations were published in the Federal Register which, among other things, would have required intrastate blood banks to use the CEP test for HBsAg. These banks collect about 40 percent of the Nation's blood supply. Interested persons had until August 26, 1974, to file written comments with FDA. As of February 1975, FDA had not implemented these proposed regulations.

In April 1974, FDA licensed another third-generation test for HBsAg. Before the licensing of that test, the RIA test was the only third-generation test licensed. According to FDA, this test--reverse passive hemoglutination--is nearly as sensitive as the RIA test.

On July 9, 1974, FDA proposed regulations which would require blood banks to use a third-generation test. Interested parties had until September 9, 1974, to comment on the proposal. According to FDA officials, both interstate and intrastate blood banks would be required to use this test. As of February 1975, FDA had not implemented the proposed regulations. Effective September 1975, after we submitted our report to HEW for comment, FDA required all blood to be tested by a third-generation test.

TESTING BY INTERSTATE BLOOD BANKS

We reviewed the latest inspection reports available in March 1974 for blood banks licensed to ship blood interstate. These reports, generally representing inspections performed

during 1972 and 1973, showed that the RIA test was used at only 83 of the 246 blood banks. The reports did not show the percentage of blood which tested positive for HBsAg. The following table shows the number of blood banks using the RIA and CEP tests and the number of units collected annually.

Tests used	Number of blood banks using test	Annual units of blood collected	Percentage of units tested
CEP only	159	3,330,900	53.1
RIA only	27	822,600	13.1
CEP and/or RIA	56	2,040,800	32.6
Not shown	4	75,900	1.2
Total	246	6,270,200	100.0

Thus, at least 53.1 percent of the units collected were tested by only the CEP method.

However, in January 1974 FDA surveyed the interstate blood banks that were collecting and testing units of blood. That survey found that 100 banks were using the RIA test, 52 were using the RIA and/or CEP test, and only 95 were using the CEP test. Thus, many were apparently converting to the RIA method.

TESTING BY INTRASTATE BLOOD BANKS

January 1973 regulations required that all blood banks register with FDA and be subject to its inspection. Of the approximately 5,200 blood banks dealing in intrastate commerce, only 957 had been inspected by FDA as of January 1974. The inspection reports for these 957 blood banks showed that 406 were collecting blood. Blood for the remaining 551 was apparently obtained from other blood banks. The reports on the 406 banks covered inspections made between March 1973 and January 1974. Of these 406, at least 246 used some test other than the RIA test or no test at all. These 246 blood banks collected an estimated 617,700 units of blood per year. The tests used and the estimated number of units collected annually by these banks are shown in the following table.

Tests used	Number of blood banks using test	Estimated annual units of blood collected	Percentage of units tested
CEP only	232	610,250	65.1
RIA only	28	46,350	5.0
CEP and/or RIA	33	150,400	16.0
Less sensitive test than CEP	4	4,150	.4
Not determinable	99	122,850	13.1
No test performed	10	3,950	.4
Total	406	937,950	100.0

BASIS FOR NOT REQUIRING RIA TESTING

According to FDA officials, blood banks were not required to use the RIA test because:

--Only one manufacturer was licensed to produce reagents for use in the RIA test and FDA questioned whether that manufacturer could meet the demand. Even if the manufacturer could meet the demand, FDA was concerned about the contingencies of labor disputes and production problems.

--About the time RIA reagents were licensed, researchers learned that many of the units detected as HBsAg positive were not actually so.

Possible lack of test materials

Until January 1975 all the materials for the RIA test were produced by one company. Officials of that company told us they had never had any labor problems in their pharmaceutical division. They also said their manufacturing capability was sufficient to supply all the RIA test kits needed to test all blood collected in the Nation.

FDA licensed the same company to produce the materials needed for another new third-generation test in April, 1974. Regulations proposed by FDA on July 9, 1974, would require blood banks to use a third-generation test.

According to HEW, regulations published in the Federal Register on July 15, 1975, require that blood banks use a third-generation test by mid-September 1975. HEW also

informed us that FDA has attempted, within practical limits, to assure prompt and efficient application of technology for HBsAg testing. Slippages were reportedly due to practical obstacles.

False positives resulting from RIA test

Shortly after the RIA test was licensed, studies showed that a considerable amount of blood that was testing positive by the RIA method and negat_ e by the CEP method was in fact negative (false positive). An FDA official said one such study showed that about 80 percent of units testing negative by CEP and positive by RIA were in fact false positives. Other such studies, however, showed lower rates.

According to the manufacturer of the RIA test materials, false positives are of two types. The first results from improper testing procedures by the blood banks; the second results from the materials used to perform the test. The manufacturer said some persons tested positive because their blood had developed antibodies to the materials used in the test (guinea pig globulin).

In June 1973 and April 1974, the manufacturer altered the formula for the testing material. According to an FDA official, false positives caused by the guinea pig globulin are now rare.

The official added that false positives caused by improper testing procedures still exist but have probably been reduced because (1) persons performing the test are more aware of the problems and (2) the manufacturer made certain changes in the testing method which reduce the chance for errors.

The false positive problem is apparently not unique to the RIA test but exists also with the CEP method. FDA periodically conducts HBsAg proficiency tests. Samples containing known HBsAg positives and negatives are sent to blood banks, which test the samples for HBsAg, record the results, and send them to FDA. These proficiency tests have shown a higher false-positive rate for CEP tests than for RIA tests. The samples do not contain antibodies to guinea pig globulin and any false positives are therefore the result of technician errors.

The results of four recent proficiency tests conducted by FDA and the percentage of false positives associated with the CEP and RIA tests are shown below.

Date of test	Number of establishments testing by		Percentage of false positives	
	CEP	RIA	CEP	RIA
Aug. 1972	256	6	0.9	-
Jan. 1973	228	47	11.8	0.5
Aug. 1973	192	108	4.4	2.4
Jan. 1974	147	152	5.1	1.2

COST AND SAVINGS OF CEP AND RIA TESTING

According to a 1973 HEW study, before FDA required HBsAg testing, 20,000 cases of overt post-transfusion hepatitis occurred each year and 1,000 of those resulted in death. It was also estimated that subclinical cases outnumbered the overt cases by five to one. A subclinical case is one in which the disease is not detected by observation although it may result in adverse long-term effects, such as cirrhosis of the liver. An overt case is one in which the patient has the disease symptoms and, according to HEW, will be disabled for about 1 to 2 months.

The study estimated that each case of overt post-transfusion hepatitis cost society $4,800--representing a total annual cost of $96 million--in hospitalization costs and lost earnings. (Physician charges and the cost of intensive care for those needing it were not included.) The study estimated that to test one unit of blood using the CEP test cost 50 cents and that 8.8 million units were collected annually and concluded that, because the CEP test was 15-percent effective, it could annually (1) prevent 3,000 cases of overt post-transfusion hepatitis, (2) prevent 150 deaths, and (3) save society about $10 million. The $10 million figure equals 15 percent (the effective rate of CEP) of the $96 million cost to society minus the $4.4 million cost of performing CEP tests on all blood.

Using data from the 1973 HEW study, we made a similar comparison of the advantages of RIA testing instead of CEP testing. Because the RIA test is twice as effective as the CEP test, it would prevent an additional 3,000 cases of overt post-transfusion hepatitis and 150 deaths and would result in a gross savings of $28.8 million annually. After the $10 million savings attributed to the CEP test and the $13.2 million cost of performing the RIA test ($1.50 per test for 8.8 million units of blood) are deducted, the use

of the RIA test would result in a net savings of $5.6 million over the savings attributable to the CEP test.

If the savings estimates had been computed on the basis of the CDC estimate (see p. 2) that post-transfusion hepatitis took 3,700 lives and cost the economy $251 million in 1970, the savings attributable to both tests would be much greater.

It should be noted that the HEW study showed the advantages of testing all blood by the CEP test as compared with no test at all and the comparison we made showed the advantages of testing all blood by the RIA method as opposed to the CEP method. The $5.6 million in additional savings attributable to the RIA test could not be claimed for requiring the RIA test by FDA regulation because some of the blood was already being tested by the RIA method.

According to our review of the latest inspection reports available at March 1974, however, at least 53 percent of all blood collected by interstate banks was apparently tested by the CEP method. Also, according to FDA inspections completed at January 1974, at least 65 percent of the blood collected by intrastate banks was apparently tested by the CEP method. Therefore, a substantial number of post-transfusion hepatitis cases could have been prevented and a substantial savings realized if the RIA test had been required.

CONCLUSIONS

Many post-transfusion hepatitis cases have been prevented since July 1, 1972, when FDA required interstate blood banks to test for HBsAg. In August 1972 FDA required blood banks to use a test method at least as effective as the CEP test. However, the RIA test was then known to be at least twice as effective as the CEP test in detecting blood carrying hepatitis. As of February 1975 interstate blood banks still were not required to use the RIA test and intrastate blood banks were not required to test at all. We believe that many cases of post-transfusion hepatitis could have been prevented with a substantial savings to the Nation's economy if FDA had required all blood banks to use the most effective test available in testing for HBsAg.

RECOMMENDATION TO THE SECRETARY OF HEW

We recommend that the Secretary develop a procedure (1) requiring all units of blood to be tested for HBsAg by the best test available and (2) designed to insure that in the future new and improved tests are implemented as soon as practicable. Factors that should be considered in determining

the best test include the test's effectiveness, its cost, and the availability of materials, to perform it.

HEW COMMENTS AND OUR EVALUATION

HEW concurred with our recommendation. On July 15, 1975, FDA published in the Federal Register regulations that became effective in September 1975, requiring all units of blood to be tested by the best test then available. According to HEW, over the past 3 years procedures have been established to assure that in the future new and improved tests will be implemented as soon as practicable.

HEW stated, however, that the lag time between FDA approval of the test and its widespread application has been remarkably short and that our report does not accurately reflect this fact. HEW indicated that manufacturers' distribution records are a better indicator of the extent to which third-generation tests are being used than are the FDA inspection reports.

In our opinion, the time lag between FDA approval of the RIA test and its use by blood banks could have been greatly reduced if FDA had required blood banks to use the test. The test was known to be twice as effective as the CEP test in July 1972, yet FDA did not require it, or other third-generation tests, until September 1975.

We disagree that manufacturers' records are a better indicator of blood banks' use of the RIA test than FDA inspection reports. The inspection reports record the test used by the blood banks at the time of inspection.

We believe that the inspection reports were a more reliable source of data. Blood banks and hospitals use the test materials for other purposes. The manufacturer records might not show whether the materials were used to test blood for HBsAg before distributing the blood or for other purposes.

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The American Blood Commission agreed with our recommendation and made no comments in addition to those made by HEW.

CHAPTER 5

BENEFITS POSSIBLE FROM FROZEN BLOOD

Scientific evidence suggests that the incidence of post-transfusion hepatitis might be substantially reduced if frozen washed red blood cells (commonly referred to as frozen blood) were used more widely. The general consensus among blood bank officials is that it is the washing of the blood cells, and not the freezing, that eliminates the hepatitis virus.

Human blood is made up of two main components, cells and plasma. Before freezing, the cells are separated from the plasma by centrifugation. A glycerol solution is then added to the cells to prevent their destruction during freezing. The cells and solution are then frozen. When the cells are needed for transfusion, they are thawed by placing the storage container into warm water. After thawing, the cells are generally washed with a saline solution to remove the glycerol.

Research to determine the effect on post-transfusion hepatitis of transfusing blood that had been frozen appears to be limited. We believe that such research should be emphasized because of the impact that frozen blood could have on the post-transfusion hepatitis problem.

INCIDENCE OF POST-TRANSFUSION HEPATITIS WITH FROZEN BLOOD

Scientific evidence suggests that the incidence of post-transfusion hepatitis would be reduced if frozen blood were more widely used. Although various scientific studies on the use of frozen blood have been published, none provide conclusive scientific evidence on the impact that freezing or washing blood has on the incidence of post-transfusion hepatitis.

An October 1970 Department of the Navy study concluded that hepatitis occurred substantially less frequently after the transfusion of frozen blood that had a hepatitis-free solution added to it for transfusion than after the transfusion of frozen blood that had the original plasma

added to it for transfusion. It is generally accepted that blood plasma can transmit hepatitis. Of 104 recipients that received 442 transfusions of frozen blood with the original plasma added, 4 developed post-transfusion hepatitis. Of 110 recipients that received 623 transfusions of frozen blood with the hepatitis-free solution added, none developed post-transfusion hepatitis. The scientific director of the organization performing the study said, however, that the study had been criticized because of the small number of cases involved.

A study made between 1968 and 1972 used some blood cells which had not been frozen but which were subjected to the same washing procedure used to remove the glycerol solution from frozen blood. The purpose of the study was to determine the effect of washed cells on post-transfusion hepatitis. The study involved Vietnam veterans at the U.S. Naval Hospital, Chelsea, Massachusetts. Most had suffered serious combat injuries requiring multiple blood transfusions and long hospitalization.

Blood samples taken from the patients after they had received their blood transfusions were tested for HBsAg by the RIA method. The following table shows the results of the study.

Type of blood transfused	Number of patients	Number HBsAg positive
Liquid whole blood	33	1
Whole blood and washed cells	44	3
Washed cells only (includes frozen and nonfrozen cells)	30	-

In a third study supported in part by Public Health Service grants, 88 kidney dialysis patients receiving transfusions of frozen blood were studied from February 1963 to September 1971. These patients received a total of 2,998 units of frozen blood, 80 percent of which were administered before the bank started testing for HBsAg. Subsequent testing of patients for HBsAg showed that none had become HBsAg positive. In addition, none showed any clinical evidence of hepatitis. Estimates presented in the study show that, had whole blood been transfused instead of frozen blood, 12 to 18 potentially infectious units would have been transfused.

These three studies indicate that using frozen blood may reduce the incidence of post-transfusion hepatitis. According to NIH officials, however, because of the limited number of studies made and the limited extent of these

studies, the evidence is inconclusive. We were also informed that NIH is not supporting any research to determine what effect freezing or washing blood has on post-transfusion hepatitis.

OTHER ADVANTAGES OF FROZEN BLOOD

To determine other advantages of using frozen blood, we gathered data and talked to officials at eight blood banks with established frozen blood systems. We also talked with (1) officials at three blood banks that were considering adopting frozen blood systems, (2) Defense Department officials involved with blood banking, and (3) researchers active in frozen blood research.

Most blood bank officials we talked to did not mention the reduction of post-transfusion hepatitis as a primary reason for using frozen blood; all, however, mentioned it as an advantage.

Originally, frozen blood was thought to be useful only for preserving rare blood types and for autotransfusions. Autotransfusion is transfusing a patient with his own blood collected in anticipation of need. Experience has shown that, besides potentially reducing the transmission of post-transfusion hepatitis, frozen blood has other benefits, some of which are described below.

Better management of blood

A frozen blood system provides better management of blood inventories by insuring a more adequate supply of blood during shortage periods. Traditionally, people tend to donate blood when it is convenient for them to do so. Therefore, during vacation periods and long holidays (such as Christmas through New Years) blood supplies often become very low. Federal regulations permit storing frozen blood for up to 3 years. It can therefore be stored when it is available and thawed and used during shortage periods.

Fresher blood

Cells frozen shortly after they are collected are better than whole blood stored for over a week. The quality of cells after thawing and washing is indistinguishable from that before freezing, whereas whole blood begins to lose its freshness after about 5 to 7 days. After 21 days blood not frozen has deteriorated to the point that it is no longer acceptable for transfusion. The high quality of frozen blood is especially beneficial for scheduling certain surgical procedures such as heart surgery, which requires

about 10 to 12 units of very fresh blood. Without a frozen blood system, the timing of such surgery is often influenced by the availability of enough donors of the correct blood type at the correct time.

Component therapy

Frozen blood promotes the practice of component therapy. Using blood components is usually far superior to using whole blood. The Committee on Transfusion and Transplantation of the American Medical Association has taken the position that when a blood transfusion is considered essential, packed cells (blood cells with most of the plasma removed) should be used rather than whole blood in almost all instances. As previously noted, the plasma is removed prior to freezing. Using red cells (white cells are destroyed during freezing, as discussed below) reduces the incidence of circulatory overload, which is probably the most common cause of transfusion injury. In addition, separating the cells from the plasma frees the plasma so that it can be used to prepare other blood products and components.

Fewer transfusion reactions

The white blood cells contain antibodies which, if transfused in sufficient quantities, can cause a patient to react adversely to future blood transfusions or can cause transplanted organs to be rejected. The glycerol solution used to protect the blood cells during freezing does not satisfactorily protect white blood cells and most of them are destroyed by freezing. In addition, according to the Committee on Transfusion and Transplantation, with less plasma transfused, less sodium and potassium citrate are given to the patient, thus reducing the risk of other transfusion reactions.

Increase in number of donors

The blood from some donors contains certain undesirable antibodies that would normally cause these persons to be eliminated as donors if the antibodies were identified before the blood was collected. If the antibodies were identified after the blood was collected, the blood would normally be discarded. Because freezing removes such antibodies, blood from such donors may be used.

DISADVANTAGES OF FROZEN BLOOD

Some researchers and blood bank officials cited a number of problems with a frozen blood system, including (1) higher cost of frozen blood, (2) more blood wasted, and (3) unavailability of frozen blood for emergency use.

Increased cost

A study prepared by the U.S. Naval Blood Research Laboratory shows the additional costs for processing a unit of frozen blood. The costs were developed for four blood freezing and processing systems over a range of from 500 to 10,000 units annually, and include costs for operating the storage freezers, solutions used to protect the cells during freezing and wash the cells before transfusion, equipment depreciation, labor, space, and additional materials. Collection costs were not included. The table on the following page shows the additional costs associated with freezing blood, according to the study.

The estimated freezing and processing costs range from a low of $34.13 per unit to a high of $81.12 per unit; such costs are less for banks that are freezing and processing large quantities of blood and do not include the normal costs of collecting and processing a unit of unfrozen blood.

As previously noted, the Office of the Assistant Secretary for Health and CDC officials estimated the economic cost of post-transfusion hepatitis for 1970 to have been $95.7 million and $251.1 million, respectively. A study prepared for the National Blood Resource Program shows that 6.4 million units of blood were transfused during 1971. By dividing the number of units transfused into the estimates of the cost to the economy of post-transfusion hepatitis, we estimate that the cost of post-transfusion hepatitis, prorated over each unit of blood, is $14.95 based on the Office of the Assistant Secretary for Health estimate, and $39.23 based on the CDC estimate. Therefore, if it can be established that using frozen blood will greatly reduce the incidence of post-transfusion hepatitis, savings to the economy could offset a substantial portion of the cost of freezing and washing blood.

Waste

Under FDA regulations, unfrozen blood must be discarded after 21 days if it is not used. Frozen blood not used within 24 hours after thawing must be discarded.

At the hospitals we visited, using frozen blood has generally resulted in better use of blood resources. At three hospitals the percentage of units lost during processing and because of the 24-hour outdating period was less than the percentage of unfrozen units discarded because of the 21-day limit. At a fourth hospital the percentage of units discarded because of outdating and technical loss declined from 5.7 percent in 1968 to 2.4 percent in 1973.

Unit Costs for Four Major Blood Freezing and Processing Systems for Volumes Between 500 and 10,000 Units Annually

Process/cost categories	500	1,000	2,000	3,000	4,000	5,000	6,000	7,000	8,000	9,000	10,000
Process A:											
Freezer operation	$ 2.12	$ 2.12	$ 1.86	$ 1.94	$ 1.86	$ 1.48	$ 1.24	$ 1.06	$ .93	$ .82	$ .74
Solutions and disposable supplies	20.67	20.32	20.17	20.17	20.17	20.17	20.17	20.17	20.17	20.17	20.17
Equipment depreciation	43.25	25.04	15.25	12.44	10.70	10.26	8.60	7.38	7.52	6.68	6.86
Labor	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Storage and lab facilities	10.08	5.84	3.87	3.21	2.89	2.38	1.99	1.70	1.62	1.47	1.36
Total	$81.12	$58.32	$46.15	$42.76	$40.62	$39.29	$37.00	$35.31	$35.24	$34.14	$34.13
Process B:											
Freezer operation	$ 2.12	$ 2.12	$ 1.86	$ 1.94	$ 1.86	$ 1.48	$ 1.24	$ 1.06	$ .93	$ .82	$ .74
Solutions and disposable supplies	30.41	30.41	29.16	29.16	29.16	29.16	29.16	29.16	29.16	29.16	29.16
Equipment depreciation	13.78	10.30	7.88	7.53	7.01	5.84	4.92	4.22	3.83	3.41	3.18
Labor	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Storage and lab facilities	9.52	5.56	3.73	3.12	2.83	2.30	1.92	1.64	1.58	1.41	1.29
Total	$60.83	$53.39	$47.63	$46.75	$45.96	$43.78	$42.24	$41.08	$40.50	$39.80	$39.37
Process C:											
Freezer operation	$ 2.12	$ 2.12	$ 1.86	$ 1.94	$ 1.86	$ 1.48	$ 1.24	$ 1.06	$ .93	$ .82	$ .74
Solutions and disposable supplies	25.20	25.20	25.20	25.20	25.20	25.20	25.20	25.20	25.20	25.20	25.20
Equipment depreciation	19.88	13.35	9.41	8.55	7.78	6.75	5.68	4.87	4.59	4.08	3.94
Labor	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Storage and lab facilities	9.80	5.70	3.80	3.17	2.86	2.34	1.95	1.67	1.62	1.44	1.32
Total	$62.00	$51.37	$45.27	$43.86	$42.70	$40.77	$39.07	$37.80	$37.34	$36.54	$36.20
Process D:											
Freezer operation	$ 3.18	$ 3.18	$ 3.18	$ 3.18	$ 3.18	$ 2.54	$ 2.12	$ 1.82	$ 1.59	$ 1.41	$ 1.27
Solutions and disposable supplies	28.05	28.05	28.05	28.05	28.05	28.05	28.05	28.05	28.05	28.05	28.05
Equipment depreciation	12.13	9.70	8.49	8.08	7.88	6.44	5.40	4.63	4.13	3.68	3.38
Labor	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00	5.00
Storage and lab facilities	11.10	6.75	4.80	4.40	4.45	3.62	3.01	2.58	2.43	2.16	1.97
Total	$59.46	$52.68	$49.52	$48.71	$48.56	$45.65	$43.58	$42.08	$41.20	$40.30	$39.67

According to a hospital official, use of frozen blood was the main reason for this decline. These four hospitals were freezing 30 percent or less of their total collections.

The only hospital reporting increased losses since initiating a frozen blood system was a blood bank that attempted to operate a 100-percent frozen blood system. During the year before the hospital began large-scale freezing, it lost 6.6 percent of available units of blood because of outdating. During the 6-month period after large-scale freezing began, 9.3 percent of the units were discarded because of the 24-hour regulation and 3.3 percent were lost during the freezing and washing process.

Unavailability for emergency use

Thawing and washing blood adds about 30 minutes to the processing time, thereby precluding its use for emergency cases. This did not appear to be a problem at any of the hospitals we visited generally because they were meeting most of their needs with conventionally stored blood.

At the hospital that attempts to operate a 100-percent frozen blood system, emergency needs are met by routinely washing type O blood, in anticipation of emergencies. Frozen washed type O blood is an acceptable substitute for other blood types. The hospital also holds blood for an average of 4 to 5 days before freezing, during which time it can be used for emergencies.

CONCLUSIONS

Scientific evidence supporting the use of frozen blood to reduce post-transfusion hepatitis is inconclusive. The general consensus is that the washing, not the freezing, apparently reduces the problem. Although many hospitals and blood banks are using frozen or washed red cells to some extent, none of those in our review adopted its use primarily to reduce post-transfusion hepatitis but consider this reduction as an additional advantage. Frozen blood provides the obvious benefit of allowing long-term storage and preservation; in addition, the medical profession has found other advantages of frozen and fresh-washed red cells, which have increased their use. There are certain problems, such as the 24-hour outdating period, that may preclude using only frozen blood. Research should be directed toward (1) determining the effects of frozen blood on post-transfusion hepatitis and (2) alleviating the problems associated with the use of frozen blood.

RECOMMENDATION TO THE SECRETARY OF HEW

We recommend that the Secretary emphasize research to

--determine the effects of frozen and fresh-washed red cells on post-transfusion hepatitis and

--alleviate the problems attributed to frozen blood systems.

HEW COMMENTS AND OUR EVALUATION

HEW concurred with our recommendation to emphasize research to determine the effects that frozen blood and washed blood have on post-transfusion hepatitis. According to HEW, NIH and FDA have been helping the Red Cross to design and implement a study to determine whether or not freezing, thawing, and/or washing red blood cells reduces the transmission of hepatitis.

HEW generally concurred with our recommendation to emphasize research to alleviate the problems attributed to frozen blood systems. HEW informed us that manufacturers active in the area of frozen blood are considering possibilities for simplifying and rendering less expensive both the equipment and labor required for these procedures. HEW stated, however, that the additional cost of freezing blood must continue to be a factor in determining the extent to which frozen and/or washed red cells should be used.

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The American Blood Commission agreed with our recommendation for additional research to determine the effects of frozen and fresh-washed red cells on post-transfusion hepatitis. It made no comments in addition to those made by HEW.

CHAPTER 6

SCOPE OF REVIEW

We conducted our review at 31 blood banks, of which 19 were in hospitals. Their locations and the annual number of units of blood they collected are as follows:

Location	Number of blood banks		Number of units of blood collected
	Hospital	Other	
Baltimore area	3	1	17,074
Boston area	5	1	216,818
Chicago area	7	6	198,798
Los Angeles area	3	4	28[illegible],617
NIH Clinical Center	1	-	4,977
Total	19	12	727,284

The 727,284 units is about 8 percent of the Nation's total annual blood collections.

We selected most blood banks for review because they (1) collected a substantial amount of blood, (2) were involved with a frozen blood operation, (3) had a high rate of hepatitis resulting from the blood they collected, or (4) had a special involvement in the hepatitis problem, such as participation in a study to determine the effects of certain agents on preventing post-transfusion hepatitis. We developed HBsAg rates at 21 of the banks, selecting them on the basis of the socioeconomic condition of the neighborhoods from which their donors came.

As a part of our review of the procedures used for reporting post-transfusion hepatitis cases, we met with officials and reviewed certain records of State and local health departments for the Boston, Chicago, and Los Angeles areas.

We also obtained information from drug treatment centers in the Baltimore, Boston, Chicago, Los Angeles, and New York areas. The New York area was included because the Department of Justice has estimated that over 50 percent of the Nation's heroin addicts live there.

In addition to our fieldwork, we reviewed (1) various records at FDA and CDC, (2) proposed legislation designed in part to reduce the post-transfusion hepatitis problem, (3) HEW efforts to establish and implement a National Blood

Policy, and (4) the effects of the Illinois "Blood Labeling Act." We also met with officials of HEW's Office of the Assistant Secretary for Health, FDA, NIH, CDC, and the Department of Defense.

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
OFFICE OF THE SECRETARY
WASHINGTON, D.C. 20201

OCT 23 1975

Mr. Gregory J. Ahart
Director
Manpower and Welfare Division
U.S. General Accounting Office
441 G Street, N.W.
Washington, D.C. 20548

Dear Mr. Ahart:

Enclosed is the revised departmental response to the Comptroller General's report entitled "Hepatitis Resulting from the Transfusion of Blood--An Evaluation of Four Methods to Reduce the Problem." By the submission of these comments, we are withdrawing our response of July 29.

The comments were revised as a result of a request from your staff for additional data in support of the Department's position concerning the National Blood Policy and our efforts to improve blood services.

We appreciate the opportunity to comment on this draft report before its publication.

Sincerely yours,

John D. Young
Assistant Secretary, Comptroller

Enclosure

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Comments of the Department of Health, Education, and Welfare on the Comptroller General's Report to the Congress of the United States, entitled Hepatitis Resulting from the Transfusion of Blood -- An Evaluation of Four Methods to Reduce the Problem. B-164031(2) April 24, 1975

October 10, 1975

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APPENDIX I

I. Overview

Observations and Conclusions by the Department in Respect to Transfusion-Related Hepatitis in the Context of Blood Services in General, and Various General and Certain Specific Aspects of the GAO Report.

Vast quantities of evidence have been accumulated attesting to the inordinately high hepatitis risk of blood derived from paid as compared to voluntary donor sources.[1,2,3,4] In every study where volunteer donor blood has been substituted for commercial blood there has been a dramatic decrease in hepatitis frequency among recipients. For example, an 82% reduction in post-transfusion hepatitis was found by the Clinical Center Blood Bank (CCBB), NIH when it excluded commercial donors and adopted a system whereby NIH employees were required to volunteer their first donation and every alternate donation thereafter; interim donations were paid. Simultaneously, CCBB initiated routine donor screening for HB_sAg; calculations[5] demonstrated that the 82% reduction was primarily attributable to rejection of blood derived from commercial sources. At the VA hospital in Hines, Illinois,[6] the change from a commercial base (92% paid donations) to a volunteer system (96% voluntary donations) resulted in a decrease in post-transfusion hepatitis from 20.8% to 7.7%. Implementation of a law requiring labelling of blood as to source has resulted in a marked increase in the percentage of voluntary blood utilized in the State of Illinois. It is anticipated that this will result in a decrease in post-transfusion hepatitis parallel to that observed in the Hines VA study, but reliable data regarding this point are not currently available.

To the present time, no one knowledgeable in the fields of hepatitis and blood banking has challenged the validity, efficacy or importance of eliminating commercial blood sources; controversy has existed only with regard to the best method of implementing such change. The American Blood Commission, whose members represent collectors of more than 85% of the nation's needs for whole blood, in keeping with the National Blood Policy, has recently adopted an all-voluntary blood system as one of its principal goals. The GAO plan to retain substantial numbers of paid donors, though undoubtedly well intentioned, is based on a misinterpretation of available data, does not represent a practicable approach, and most important, would not achieve its declared goal—a significant decrease in post-transfusion hepatitis. Indeed, the proposals, relying on HB_sAg prevalence and post-transfusion hepatitis incidence to qualify voluntary and paid donor populations, might actually result in an increase in such hepatitis and would do so at great cost to the Government, while increasing, not decreasing, the cost of blood services throughout the country. In this situation, we believe the burden of proof must fall on GAO to establish that such a system would be practical, safe, and effective. Its draft report fails to provide such proof or to suggest that such proof will be, or can be, forthcoming.

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The essence of the GAO report is, we believe, based upon 3 observations which we propose to examine carefully in the following paragraphs.

That some paid donors are as safe or safer than some volunteer donors. We agree that payment, in itself, does not make a donor a hepatitis risk and indeed that there are some paid donors who are as safe or safer than some voluntary donors. However, as stated above, the data are overwhelming that paid donors, as a group, carry a significantly greater risk of transmitting both hepatitis B and "non-B"[7] than donors who are not paid. Despite a few exceptions, persons who are sufficiently motivated to donate their blood are more likely to belong to a socio-economic class in which the hepatitis risk is relatively low.[8] Numerous efforts have been made to find means of identifying appropriate measures of socio-economic status which would be acceptable to people who are being asked to provide a gift of blood. To date, the most acceptable means seems to be that of the basis for the gift, which is to say whether the gift is made freely and without remuneration or some form of material inducement.[9] Alternatively, one might, with trepidation, question prospective donors of blood as to their annual income level. We would submit that the experience of the Federal Government in respect to income tax and the confidentiality of taxpayers' declaration militates against such an approach. We are reasonably confident that questions of this nature would have an adverse impact upon voluntary donors. By contrast, it is to be expected that falsification of statements on matters of income would be readily supplied by drug addicts.

When one pays donors there is no reliable and widely applicable way to distinguish the "good" paid donor from the "bad" paid donor (see below); since it is clear that a high proportion are "bad", it is much the safer course to insist on all-voluntary donor blood. The GAO report also claims that there is a difference in "hospital paid donors" compared with commercial paid donors. This is undoubtedly true, in some instances, but if one were only to eliminate commercial blood banks, these same undesirable donors would be expected to gravitate to hospital blood banks and might change the donor status of these institutions.

It has been estimated that only 11%* of blood units in America are derived from commercial sources, but that this 11% accounts for a major portion of post-transfusion hepatitis. There is no measure currently available which could make such a significant inroad into post-transfusion hepatitis, at such minimal cost, as would elimination of the paid blood donor.

That the elimination of paid donors could cause blood shortage problems. This fear might be well-founded if the tactic for attaining an all-voluntary system called for proscription on the use of purchased blood and allowed the

*National Heart Lung Institute Blood Resource Study; Supply and Use of the Nation's Blood Resource. 1: 56, 66-68, 1972

voluntary sector no period for expansion of its supply system. In fact, the tactic for achieving an all-voluntary supply under the National Blood Policy calls for expanded recruitment of voluntary donors and a corresponding increase in the supply of voluntarily donated blood, such that there would be no need for purchased blood. This tactic ties the diminution in reliance on purchased blood to the sufficiency of the supply of voluntarily donated blood. This approach has been highly successful in Cleveland, Rochester (New York), Seattle, San Francisco, the State of New Jersey, and that part of the Southwest served by Blood Services, Inc. It is particularly noteworthy that the State of New Jersey has moved from 36% commercially acquired blood in 1969 to 0.049% in the second quarter of calendar year 1975,[10] and that the Northern Ohio Red Cross Blood Program, centered in Cleveland, increased its voluntarily donated blood from 85,000 to 132,700 units per year during the period 1972 to June 30, 1975. This now accounts for more than 70% of the blood needs of the Greater Cleveland area.[11]

Chicago has employed a different tactic because a relatively recently enacted State law requires the labelling of purchased blood as to source. Nonetheless, Chicago has met its needs for voluntarily supplied blood with some assistance from surrounding areas, and it is rapidly becoming self-sufficient. The State of Illinois as a whole attained a 98% voluntary blood donor supply in 1974.

The GAO's references to experience at the Clinical Center Blood Bank (National Institutes of Health) merit comment. The suggestion that problems have arisen because the blood bank ceased to pay donors is incorrect. Both the gain of donors following institution of a paid donor system at NIH and the relatively small loss of donors following cessation of this system were predicated upon many variables, including the adoption of a computerized donor retrieval system, variations in the magnitude of donor recruitment campaigns and changes in the donor population due to abolition of the military draft. The 14% reduction in donors which occurred with cessation of payment began while payment was still in use. Importantly, the Clinical Center has been able to obtain sufficient blood from voluntary donors to meet its needs, notwithstanding the appearance of recruitment messages that have been published and will continue to be published in the NIH Record.

There are other, more substantial arguments to negate GAO concern that blood availability would be significantly affected by cessation of a paid donor policy:

First, only 5-10% of those eligible to donate actually do so. There is thus a huge untapped reservoir of potential volunteer donors. If only an additional 2% of the general population were induced to donate by intensified donor recruitment programs, this would entirely compensate for the loss of commercial sources, as has already been done successfully in many areas of the country, including Rochester (New York), Chicago,

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Seattle, San Fransieso, the State of New Jersey, and that part of the Southwest served by Blood Services, Inc. It is particularly noteworthy that Blood Services, Inc., formerly a commercial collector of blood, has converted to an all-voluntary supply (99%) over a period of 3 years.

Second, the loss of high risk commercial blood could be totally offset by programs which encourage better blood utilization, including a decrease in unnecessary single unit transfusions, the use of plasma expanders rather than whole blood, the use of heart-lung machines with smaller priming volumes, a change in philosophy away from the concept of normalizing the hematocrit prior to surgery, increased use of autotransfusion, and efforts to increase the storage life of banked blood inventories.

Third, it is our belief that those donors who are currently paid but who are of a socio-economic class with a relatively low hepatitis risk (i.e., "good" paid donors) are the donors most likely to be convinced of the need for voluntary donation when they are adequately informed of the need for their donated blood and the significant effect paid donations have on post-transfusion hepatitis and on the safety of blood in general.

That the frequency of HB_sAg in a donor population can serve as a reliable indicator of the hepatitis infectivity risk of that population. The GAO report places reliance on tests for HB_sAg not only as a means of excluding the carriers of this antigen, but as an index of the relative infectivity of entire donor populations and as a potential standard of blood bank performance to the extent of determining whether or not a blood bank should be licensed. Such inferences appear to go well beyond available data and result in conclusions which we find are scientifically unsound. Several other factors relating to HB_sAg come into play. First, except for one study,[12] which does claim a significant reduction in post-transfusion hepatitis based on HB_sAg testing alone, it has been the general consensus that testing for HB_sAg has had only minimal impact on post-transfusion hepatitis. In the Hines VA study previously cited,[6] "despite the institution of screening of blood for the hepatitis B surface antigen in August 1970, the total incidence of hepatitis did not decrease." In contrast, a change to voluntary donors in this same hospital resulted in a 62% decrease in post-transfusion hepatitis. Dr. Polesky of the Minneapolis War Memorial Blood Bank has recognized an increase in hepatitis despite HB_sAg testing.[13] Several studies[5,14] have estimated that, at a maximum, testing for hepatitis B antigen would decrease post-transfusion hepatitis by no more than 25%. Although these studies were done with slightly less sensitive tests than are currently available, they were also done at a time when HB_sAg-positive donors had not yet been purged from donor files and thus at a time when more transfusion hepatitis would be HB_sAg-related than it is at present. Even with RIA testing, the maximum impact on post-transfusion hepatitis attributable to the exclusion of HB_sAg-positive donors would be a 25% reduction.[15] This is not to suggest that testing should not be performed, but to place HB_sAg testing in its proper

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perspective and to show that it has a minor role in reducing post-transfusion hepatitis as compared with the impact produced by excluding paid donor sources. In addition, if one employs a donor population which is screened for HB_sAg by RIA, it can be shown that approximately 90% of the residual hepatitis is unrelated to the hepatitis B virus and hence independent of tests for HB_sAg.[15] Thus, the frequency of HB_sAg in an RIA-tested donor population is an unproven predictor of the infectivity of that population and may be quite misleading. In contrast, it has been shown that non-B hepatitis is more common following paid blood just as is type B hepatitis.[7] Thus, eliminating commercial donors should also decrease "non-B" hepatitis, a reduction that would be totally independent of HB_sAg detection and not necessarily reflected in the frequency of HB_sAg in donor population.

Other factors being equal, those blood banks employing the most sensitive tests with the highest proficiency would be considered the poorest performers under the CAO proposal. Under exhortation by the Government to achieve low positivity rates among their prospective donors, such blood banks would be forced to pre-screen their donors before allowing them actually to donate blood. This would not obviate a need to test for HB_sAg each unit of blood actually drawn and would not alter anything but the blood bank's positivity rate for its actual donors. This would be a worthless and needless complication of their blood donor recruitment and blood collection activities. On the other hand, donor recruitment programs designed to appeal to the voluntary donor provide an initial screen that is without cost and is actually effective in preventing the transmission of hepatitis.

Still another problem would emanate from relying heavily on HB_sAg-testing. The prevalence of postive reactors in a donor population can be established truly only the first time that the population is tested. Subsequently, the population will be a mixture of tested individuals who have donated previously and untested first-time donors. The prevalence of positives will be higher in the latter than in the former under most circumstances, and therefore the overall prevalence will be heavily influenced by the relative proportion of repeat and first-time donors in the population. "Approving" blood banks on this basis would encourage their use of repeat donors and discourage their efforts to recruit new donors. This would be counter-productive.

The CAO does not take into account the number of repeat donors in making its assessment of individual blood banks on the basis of maximum permissible levels of HB_sAg. Indeed, no guidelines for establishing maximum permissible rates can be identified on a rational basis. The maximum permissible rate would have to vary from one geographic region to another as does the actual prevalence of HB_sAg-positivity. It is not at all clear what constructive measure could be taken by a blood bank actually found to have HB_sAg-positivity

rates above the maximum, but some might be inclined to measures which would improve the appearance of the performance. The measures proposed in the GAO report would effectively reject entire donor populations where they exceed arbitrarily established limits, limits that have yet to be determined on a data basis that has yet to be established.

In summary, if HBsAg testing could detect all or even a large majority of infectious donors, then the GAO conclusions might be justified. In reality, however, HBsAg testing detects only a minor portion of infectious donors.

The third measure proposed by GAO to maintain control over blood collection is to establish limits for, and periodically review the frequency of post-transfusion hepatitis emanating from a given blood bank. While this is a desirable goal, it is unrealistic. Many problems relate to establishing the frequency of post-transfusion hepatitis. First, the majority of cases are anicteric and relatively asymptomatic and will only be detected by periodic determination of liver function abnormalities. Yet, despite the fact that these cases are relatively benign in the acute phase, they may have significant long-term morbidity and terminate in fatal cirrhosis.* Second, as stated in the GAO Report, the reporting of even overt hepatitis cases is notoriously bad and approximates only 10%. Third, the long time lag between transfusion and the onset of hepatitis makes recognition of the causal association difficult and means that often the recipient is far away from the place of transfusion at the time hepatitis ensues. Lastly, blood from multiple donors is used in many transfusion situations and when blood comes from several blood banks, attribution of responsibility cannot be made with certainty. The only way to truly assess the hepatitis risk of a donor population is to initiate prospective studies which include periodic blood samples from blood recipients. These studies are extremely difficult and costly to perform. Were the Government to regulate blood banks by monitoring hepatitis rates in recipients, two million patients receiving seven million units of blood distributed by over 6,000 blood banks would have to be identified each year and followed individually with serial biochemical tests for not less than six months. Booz, Allen and Hamilton has done a feasibility analysis for the National Heart and Lung Institute to determine the practicality of performing prospective post-transfusion hepatitis studies involving a limited number of hospitals in order to obtain an indirect estimate of the national incidence of post-transfusion hepatitis. The projected studies to obtain the national incidence would involve 23,000 transfused patients and 23,000 non-transfused patients in 40 hospitals, over a period of 3 years. The cost of this study is projected in excess of 10 million dollars. From this information it is clear that studies of this nature are expensive. It is not clear how much it would cost to follow 2 million transfused patients treated in more than 7,000 hospitals on a yearly basis, but it is clear that the figure would be very large indeed.

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If blood banks themselves were to perform the patient followup, one would have to establish a mechanism to evaluate the completeness of their recipient followup and the validity of their reported results. As with HB_sAg testing, such a system would penalize those blood banks conducting the most complete patient followup and encourage blood banks to consciously or unconsciously fail to look for or report post-transfusion hepatitis so as not to lose their licenses. There would thus be a strong negative incentive which would compound the current gross inefficiency in determining the frequency of post-transfusion hepatitis attributable to any given blood bank.

Finally, there remain the problems posed by the disease itself. A uniform basis for the diagnosis of hepatitis would have to be established. This could be done but it could not be applied universally, because it would be virtually impossible to obtain blood samples for analysis, weekly or monthly for periods of about six months, on two million patients receiving blood transfusions. If a uniform basis for the diagnosis of hepatitis were defined but could not be applied universally, there would be no basis for comparison of performance among blood banks. Each blood bank must strive to achieve the lowest level attainable within the realities of the local situation.

Because patients frequently receive massive transfusions in one geographic location and their post-surgical care and followup in another, there would be substantial difficulty in relating actual cases of hepatitis to the source of the causative agent. The cost of following all recipients of blood and identifying all cases of transfusion-related hepatitis would be very great and an equitable means for distributing the charges for such activities has not been identified.

In summary, the proposal to monitor hepatitis rates of individual blood banks would lead to expenditure of great amounts of money for no certain benefit, on the basis of a concept (maximum acceptable limit for diseases which are conceivably preventable) which is itself unacceptable to a Department charged with responsibility for preventing preventable diseases. In addition, it would place HEW in the untenable position of spending vast sums primarily to assure access to a generally undesirable class of blood donors, and it would do these things to the detriment of an all-voluntary system which would assuredly provide the largest attainable improvement in this situation.

We have dealt to this point with the major issues in the GAO report. However, other issues require additional comment:

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A. Uniform Criteria for Donor Exclusion

While this is an objective that is wholly desirable, it is extremely difficult to achieve. For example, those who donate frequently will inevitably become "involved" in more cases of hepatitis than those who do not. Simple statistical correlations could disqualify donors who are not actually virus carriers.

The American Blood Commission's efforts to achieve commonality of practices in blood banking will undoubtedly give high priority to uniform criteria for donor exclusion within the context of total needs.

B. Mandatory Reporting of Hepatitis Cases

Mandatory reporting of hepatitis cases and HB_sAg-positive individuals by hospitals and physicians is desirable from the health viewpoint. However, reported cases must be confirmed to be HB_sAg-positive and/or to have viral hepatitis rather than other causes of liver function abnormality if confusion is to be avoided.

C. Federal Registry of Disqualified Blood Donors

There is a need to improve the mechanism by which cases of post-transfusion hepatitis are reported back to the collecting blood bank and by which information about disqualified donors is shared among blood banks. The question is how to do this. GAO recommends that the Federal Government establish a registry of unacceptable donors. This poses a series of problems that, taken together, argue persuasively against this proposal. If the registry is maintained by the Federal Government, and especially if it is maintained on a national basis, important issues of the right to privacy are raised. The provisions of the Privacy Act might require that potential donors be fully informed of all uses that may be made of the information to be gathered from the donor's blood and history; donors might be deterred if they were told that a Federal registry of disqualified donors would be the repository of negative information about them. The next effect could be a serious reduction in blood collections. Finally, thoughtful and experienced blood banking experts have argued that it may not be cost-effective to check every potential donor against a national registry of disqualified persons. Without freedom to use a universal code number system, such as the Social Security number system, a national registry may be cumbersome to the extent of being unworkable, yet use of such a code number system might be in conflict with the intent of the

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Privacy Act. The validity of these concerns must be settled before embarking on the creation of a Federal registry which undoubtedly would be costly.

Within the next two months, FDA is expected to issue final Good Manufacturing Practices for blood banks. These GMP's will include a requirement for improved recordkeeping including records of donor identity and the ultimate fate of collected units. These measures should allow the establishment of a sound donor-recipient link mandated by FDA to identify donors who should not donate, and will permit experimentation with regional registries in the private sector to ascertain under what conditions these may be cost-effective. Privacy can be better protected in such a private-sector regional system, with information-sharing among regions through the American Blood Commission rather than in a Federal national registry. Moreover, basing the information systems regionally would allow regional characteristics (likelihood of hepatitis vs. need for blood) to be influential in determining the criteria for donor disqualification.

D. Blood Bank Warning Re Drug Addicts

The GAO report deals extensively with studies related to drug addicts. The report recommends that the Secretary make GAO's findings with respect to drug addicts donating and selling their blood known to blood banks and stress the importance of not accepting them as blood donors. It is standard practice to include questions about drug addiction in donor interviews and to select only those who give a negative history and who have no evidence of venipuncture scars suggesting addiction. Although the basic rules may be broken by some blood banks, addicts may obviously prevaricate when being interviewed, and the level of vigilance might be improved, there is no lack of awareness in blood banking of the high hepatitis risk associated with drug addiction.

The GAO survey of addicts requires some additional comment. Because of the methodology, one must question the results of the survey. Without supportative data to the contrary, and in the views of the Center officials themselves, addicts would have many sound reasons for not donating or selling their blood. Addicts receiving treatment at the Centers could have felt a social pressure to give socially acceptable answers; i.e., that they have donated blood or plasma. No provision was made for addicts who did not wish to participate in the questionnaire study. If they felt obliged to fill out a questionaire, the inclination to give socially acceptable answers might have been greater, particularly if their answers could be identified with them by Center personnel.

Since addicts are notoriously unreliable sources of information, the accuracy of this survey must be questioned. Verification of claimed

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donations would have been helpful. There is no question that addicts will attempt to sell their blood. However, those with a history of hepatitis would have had to misrepresent their histories at the time of donor interviews. This must be borne in mind in evaluating statements made by the addicts concerning the sale of blood and, even more so, donation of blood. There is no doubt that both occur; the former would be eliminated by discontinuing payment for blood. The latter requires a more painstaking evaluation to quantify the problem. For example, it would be extremely important to know how many donations by addicts occurred while they were either in prison or in military service. Both circumstances are potentially obfuscating with regard to motivation for blood donation.

E. Use of Most Sensitive Test for HB_sAg

The Food and Drug Administration has attempted, within practical limits, to assure prompt and efficient application of this technology for HB_sAg testing. Admittedly, there has been some slippage due to practical obstacles. The most sensitive detection method currently available is inoculation of susceptible chimpanzees. Obviously, this will never be a practical test, and there may be other highly sensitive but, for various reasons, highly impractical methods developed. In fact, a very sensitive test for anti-hepatitis B core antigen may already fall in this category, although further evaluation is still necessary.

The record for lag time between test development, FDA approval, and widespread application has been remarkably good to date, a fact which the GAO report does not accurately reflect. A better indication of the extent of use of third generation testing, for example, could be obtained by examining the manufacturer's distribution records and several other reliable sources that were not included in the GAO report.

In July 1974, the Food and Drug Administration proposed that third generation testing be required and the Food and Drug Administration issued final rule-making on July 15, 1975, with an effective date of mid-September 1975.

F. Research on Frozen Blood

The applicability of red blood cell freezing to delivery of blood services is an extremely complex issue involving many scientific and economic considerations.

Controlled, prospective studies employing frozen blood are extremely difficult to perform. To date, there has been only one such study16

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and because of the low virucidal inactivity of hepatitis and cold sores of subjects, this study did not demonstrate a significant difference between Group and Control Group. A subsequent study by these same authors was completed by the Blood Transfusion Branch of NIH, but so few patients were entered into the study that further use discontinued. A massive clinical study has recently been published in Japan with support from the American Red Cross and advice from NIH and FDA. Basic research are currently in progress involving collaboration between the Red Cross, FDA, and PHS. Hopefully, new data on the impact of newly devised and safe inactivation will become available from these studies in the next several years. Because of the great economic impact on the nation's blood resource, which conversion to an all fresh frozen system would exert, universal use of this measure must be undertaken only if it is demonstrably beneficial and feasible.

In summary, during the past five years enormous strides have been made in our understanding of viral hepatitis, in general, and post-transfusion hepatitis, in particular. There is currently no definitive way to distinguish between the good and the bad blood donors. It follows that, by far, the safest, most feasible post-fractionation donation policy, and the one with the greatest benefit-to-risk ratio, is to exclude the one donor which has been shown epidemiologically to be deleterious, namely the paid donor. Addition of the best specific hepatitis antigen (HBAg) detection by a method comparable to RIA to a carefully voluntary supply will provide the maximum nationwide reduction in post-transfusion hepatitis that is now possible. There will still be an irreducible minimum of hepatitis cases the majority of which will have to await further refinements in testing for both type B and non B viral agents and/or the development of methods of viral removal or inactivation which would be fundamental breakthroughs.

At present, no technologic measure even approaches the potential impact on post-transfusion hepatitis that is promised by the establishment of an all-voluntary donor system. Adoption of certain of this report's recommendations would impede the progress being made in this direction. We trust that the information supplied herein will provide new impetus toward the goals of the National Blood Policy.

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DEPARTMENT'S COMMENTS RESPONDING TO SPECIFIC GAO RECOMMENDATIONS

GAO Recommendation

That the Secretary of HEW establish for blood banks, maximum acceptable rates of positive findings of HBsAg.

Department Comment

We do not concur because the principal purpose of the proposal is to retain access to a donor population having a known disproportionately high risk of transmitting hepatitis, a population that is not needed to assure a sufficient supply of blood; because the proposed measure is not demonstrably feasible as a means of actually improving the quality of blood collected; because the concept of "acceptable" maximum rates would be incompatible with the responsibilities and goals of the Departments; because a basis for establishing "acceptable" maximum rates gives identification; because the penalty to those blood banks applying the most rigorous tests with highest proficiency would be counter-productive; because a feasible means of assuring compliance has not been identified; because the financial costs of the measure, though not estimated by GAO, would be very great; and because the measure would not be cost-effective by any measure.

GAO Recommendation

That the Secretary of HEW establish for blood banks maximum acceptable incidence rates for actual cases of post-transfusion hepatitis resulting from the transfusion of blood collected by participating blood banks.

Department Comment

We do not concur because no incidence rate of post-transfusion hepatitis is acceptable (our goal is maximum prevention everywhere and we shall continue to strive to attain it by all feasible means); because an acceptable means of identifying an accurate proportion (or all) cases of post-transfusion hepatitis is lacking and cannot be developed in the foreseeable future; because maximum acceptable rates cannot be defined for either general application or application to response to particular blood banks; because a universally applicable method of linking post-transfusion hepatitis

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cases to particular sources of blood will not be available in the foreseeable future; because the measure would act as a disincentive to discover post-transfusion hepatitis cases, and this, in turn, would hamper the performance of the more conscientious operators of blood banks; similarly, because the measure would act as a disincentive to discover post-transfusion hepatitis cases, it could conceivably hinder the discovery and treatment of sub-clinical cases; because there is no feasible means of assuring compliance; and because the fiscal cost of the measure to patients and to the regulating organization is expected to exceed the potential value. In brief, this measure lacks demonstrable feasibility, almost certainly would not be cost-effective, and certainly would be counter-productive.

GAO Recommendation

That the Secretary of HEW periodically review the HBsAg positive rates of blood banks and the cases of post-transfusion hepatitis resulting from the transfusion of blood collected by the banks to ensure that they are within the established limits. The extent and priority in scheduling these reviews should be determined based on factors which show a high correlation with post-transfusion hepatitis, such as the percent below poverty level of the donor's neighborhood, whether the donors are paid or volunteer, and any factors identified by HEW.

Department Comment

We do not concur for the reasons given in the previous comment.

GAO Recommendation

That the Secretary of HEW delete from the National Blood Policy the provision calling for the elimination of the practice of purchasing blood from donors and, in its place, require each blood bank to stay within the limits established for 'hepatitis B antigen positives' and for cases of hepatitis resulting from the blood they collect.

Department Comment

We do not concur because the evidence now available overwhelmingly demonstrates that more can be done to prevent transfusion-related hepatitis by total reliance on unpaid donors than by any other

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single measure or combination of measures; because this will remain true until much more reliable technologic means have been established for screening out or "cleansing" units of blood contaminated with any transmissible infective agents that are more prevalent among those disposed to sell their blood; and because reliance on "acceptable" rates of HB_sAg positivity is demonstrably unsound. The Department finds unacceptable any suggestion that regulation should be predicated upon levels of human illness and death that are arbitrarily established as acceptable. Further, we believe that the vast majority of organizations and individuals associated with blood services in the United States, ranging from donors and collectors of blood, through processors and transfusers of blood, to potential recipients of blood, reject the practice of commerce in blood and other human tissues on health or ethical bases. We believe this because the three largest blood banking organizations in the United States, collecting about 89% of the nation's needs for whole blood, are committed to voluntary supplies of blood for transfusion purposes;[17] because the American Blood Commission was established to implement the National Blood Policy and the numerous national organizations elected to join the Commission were fully aware of the purposes of the Commission and do represent a very broad spectrum of society in the United States; and because the Blood Resources Panel of the National Heart, Blood Vessel, Lung and Blood Program stated to the National Heart and Lung Institute on April 6, 1973, in a document on voluntarism, that "The Panel, recognizing the merits of the lowered cost and increased safety of voluntarily donated blood, is of the opinion that an even more cogent reason for preferring voluntarism is the ethical one. It is important, as noted by Professor Titmuss, to encourage every opportunity for altruism. A society which cherishes the worth of the individual and fosters a high sense of social responsibility cannot set a price on human organs and tissues. Giving blood is regarded as a much needed manifestation of man's humanity to man, to be fostered quite apart from any financial or medical advantages."[18]

The Department finds contrary to the public interest the suggestion that it should ignore all of the foregoing considerations and change a well-founded policy to assure the future of commercial enterprises that contribute disproportionately to human illness, suffering, and death, and add to the burden of the health care system.

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GAO Recommendation

That the Secretary of HEW make GAO's findings, with respect to drug addicts donating and selling their blood, known to blood banks, and stress the importance of not accepting them as blood donors.

Department Comment

We concur. Although it is standard practice to avoid accepting blood from drug addicts, continuing vigilance is needed to screen them from the donating population. This is especially true because drug addicts are motivated to obtain money to support their drug habits and, in many cases, find it necessary to sell their blood. As long as payment of donors and drug addicts co-exist, this problem will continue. Accordingly,

a) FDA will maintain the highest practicable level of vigilance in FDA's compliance activities in all blood banks.

b) DHEW will work more closely with the organizations of blood bankers to increase their awareness and their level of inspection of donors for evidence of addictive practices, and to discourage use of those donor incentives which appeal especially to those who use drugs and alcohol in harmful ways.

c) DHEW will call upon the American Blood Commission's Task Force on Donor Recruitment for suggestions and actions to decrease blood collection from drug addicts.

GAO Recommendation

That the Secretary of HEW establish a Federal registry of unacceptable blood donors and periodically disseminate the registry to blood banks for their use.

Department Comment

We do not concur in this context. The Privacy Act would require that all potential donors be fully informed of all uses that may be made of the information to be gathered from the donor's blood and history. Such a requirement would act as a deterrent to donors. The effect of this could be a serious reduction in blood collections.

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A single nationwide registry almost certainly would be cumbersome and needlessly expensive.

Wanting to explore the feasibility of donor registries in a setting without these risks, we are fostering through the American Blood Commission, the development of mechanisms for sharing information and other resources within the private sector on regional bases. We are encouraging maximum creativity in the design of these mechanisms and arrangements and the fullest possible sharing of useful information of all types. Obviously, this should include the identity of donors who are considered unacceptable. The Commission will be asked to consider each of the specific suggestions associated with this GAO recommendation and take appropriate action in concert with the FDA.

GAO Recommendation

That the Secretary of HEW develop a procedure that would require all units of blood to be tested for HBsAg by the best test that is available

Department Comment

We concur. FDA has published in the Federal Register on July 15, 1975, its final regulation which will require all units of blood to be tested by the best test now available. It is to be noted that the best test is not necessarily the most sensitive test; for example, the most sensitive test at the present time would involve highly sophisticated studies in chimpanzees and is clearly not capable of being applied generally. The best test in this situation is the test which is most sensitive yet compatible with practical widespread application.

GAO Recommendation

That the Secretary of HEW develop a procedure designed to assure that in the future new and improved tests are implemented in the shortest time practicable.

Department Comment

We concur. Such procedures should exist but we assert that they have been put in place over the past three years and that the public is now and will continue to be the beneficiary of diligent efforts to apply technologic advances in this area as promptly as is practicable.

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GAO Recommendation

That the Secretary of HEW emphasize research to determine the effects that frozen blood and washed blood have on post-transfusion hepatitis.

Department Comment

We concur. The existing evidence of efficacy of freezing and thawing of red blood cells in preventing post-transfusion hepatitis is inconclusive. NIH and FDA have been collaborating with the Red Cross in its effort to design and implement a study to determine whether or not freezing, thawing, and/or washing of red blood cells reduces the transmission of hepatitis by blood. This study is being conducted in Japan because the prevalence of hepatitis is probably sufficiently high in that country to overcome some of the problems encountered in similar such studies conducted in the United States.

GAO Recommendation

That the Secretary of HEW emphasize research to alleviate the problems currently attributed to frozen blood systems.

Department Comment

We concur, but have reservations about the extent to which frozen systems may be expected to achieve wide practical application. At present, it appears that the largest potential benefit to human health that might be forthcoming from freezing, thawing, or washing, or a combination of such treatments of red cells, is the prevention of transfusion-related hepatitis. In anticipation of this possibility, the instrument manufacturing companies active in this area are considering the various possibilities for simplifying and rendering less expensive both the equipment required for these procedures and the labor involved in processing red cells in these ways.

The Department is now initiating studies to anticipate the various possible outcomes of studies of the effects of freezing, thawing, or washing of red cells on the transmission of hepatitis. The particular studies we have in mind would attempt to define the fiscal and logistical accommodations which would be necessitated by various possible outcomes with respect to hepatitis diminution or prevention.

Excluding for the remainder of this discussion the issue of hepatitis prevention, the extent to which freezing and thawing and/or washing

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of red cells should actually be practiced on a nationwide basis, locale by locale, will be determined by many complex variables which have yet to be fully defined. These variables certainly include but are not limited to the impact of these special procedures on the shelf life of blood and the expense of providing such services. Expense must continue to be a factor in this matter because the procedures necessarily consume more materials and involve additional equipment and labor-intensive activities. Unforeseeable technologic advances of a spectacular nature conceivably could modify this situation but are unlikely to completely invalidate this observation.

The American Blood Commission's newly formed Task Force on Regionalization will be addressing such matters and is expected to provide information which would be useful in allocating resources to the alleviation of the problems raised.

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GAO ANALYSIS OF HEW'S COMMENTS ON PROPOSALS MADE IN CHAPTER 2

USING DIAGNOSED CASES OF POST-TRANSFUSION HEPATITIS TO REGULATE BLOOD BANKS

HEW agreed (see app. I) that establishing limits for, and periodically reviewing, the frequency of post-transfusion hepatitis emanating from a given blood bank would be desirable, but gave the following reasons for not doing so:

--No incidence rate of post-transfusion hepatitis is acceptable. HEW's stated goal is maximum prevention of a disease and the concept of our proposal--regulation on the basis of maximum acceptable rates--would be inconsistent with the Department's responsibilities and goals.

--Most post-transfusion hepatitis cases will be detected only by periodic determinations of liver function abnormalities, which would have to be performed for all blood recipients and would be extremely difficult and costly.

--The reporting of overt cases of post-transfusion hepatitis is notoriously bad; regulating on the basis of actual cases reported would act to encourage blood banks not to report cases so as not to lose their license.

--The fiscal cost of the measure to patients and to the regulating organization is expected to exceed the potential value.

--Blood from multiple donors is used in many transfusion situations and, when blood comes from several blood banks, responsibility for hepatitis is uncertain.

With present testing methods, post-transfusion hepatitis cannot be eliminated entirely. Therefore, establishing limits of post-transfusion hepatitis for blood collected by specific blood banks would not appear to conflict with HEW's goal of maximum prevention. Establishing and complying with such rates is, in our opinion, a much more reasonable basis on which to regulate blood banks than converting to an all-voluntary donation system with no controls over the blood to prevent post-transfusion hepatitis except testing for HBsAg. As shown on page 15, some voluntary blood banks have high

HBsAg rates; these banks would continue to operate under HEW's policy.

We recognize, however, that because not all diagnosed cases of post-transfusion hepatitis are being reported to CDC, regulation on such a basis is presently impractical. HEW agreed to examine the reporting problems in connection with the establishment of a donor registry. (See p. 37.) If the reporting of post-transfusion hepatitis cases can be improved, we believe that HEW should seriously consider regulation on this basis. Until a determination can be made on establishing a reliable reporting system, we believe that the available information on diagnosed cases, together with the other indicators which show a correlation with hepatitis, should be used to establish priorities for and frequency of inspections of blood banks and to offer suggestions for changes in practices to improve blood quality.

We discussed the difficulty and cost to perform tests for all blood recipients with FDA officials and explained to them that our proposal was not intended to suggest testing all recipients. As a result of this discussion, we changed our proposal from one of establishing maximum acceptable incidence rates for all cases of post-transfusion hepatitis to one covering only diagnosed cases. HEW was notified of this change on June 12, 1975. Under our revised proposal, not all persons receiving a transfusion would be tested to determine if they contracted hepatitis. The maximum limits would apply only to persons contracting hepatitis severe enough to require hospitalization or a doctor's attention. Such cases presently are required to be reported (see p. 26), but not all cases are reported. The system needed to report and establish an acceptable limit is available, however, and greater use could be made of it and more emphasis placed on reporting to CDC all cases of post-transfusion hepatitis.

Regarding HEW's comment that regulating blood banks on the basis of actual cases of post-transfusion hepatitis would encourage them not to report such cases, we note that the present reporting system is directed toward reporting not by blood banks, but by State and local health departments, which obtain the information from doctors and hospitals.

Concerning the cost of the system, the maintenance of a donor registry (as described in chapter 3) should provide the necessary information on diagnosed cases of post-transfusion hepatitis. Also, FDA is currently required to inspect blood banks periodically. During these inspections information reported through the donor registry system and on hand at the blood banks could be used to develop actual

rates of diagnosed cases resulting from blood from the various banks.

With respect to the multiple donor problem, we believe that when a recipient contracts post-transfusion hepatitis and the blood was supplied by more than one blood bank, the banks should share responsibility in the same proportion that they supplied the blood. For example, if a patient received two units of blood from two blood banks, each bank would be assumed to have caused one-half the case. This is generally the procedure used by blood banks to evaluate whether an individual is qualified to give blood if his blood was used in a multiple transfusion after which the recipient contracted hepatitis. (See p. 30.)

If a reliable system for reporting post-transfusion hepatitis cases can be established, HEW could establish a limit of post-transfusion hepatitis cases for specific blood banks above which the banks' operations would be considered unacceptable. HEW could establish a period of time during which blood banks exceeding these limits would have to improve their blood quality.

If no improvements were made, HEW could, in a proper regulatory framework, revoke the licenses of nonconforming interstate blood banks and seek to prevent intrastate blood banks from disseminating blood suspected of containing hepatitis virus. During this period HEW should make known to blood banks various means for improving blood quality, such as drawing blood from better socioeconomic neighborhoods, using a donor registry before accepting donors, better screening blood donors, and encouraging repeat donations from donors with a low risk of transmitting hepatitis.

For example, as previously noted, seven hospital blood banks for which we developed HBsAg positive rates used paid donors. Five of them screened donors by limiting payment to members of a specified group. The HBsAg rates for the five banks using controlled groups were 0.0, 0.8, 1.4, 2.1, and 2.2 per 1,000.

In contrast, the HBsAg positive rates for the two banks which did not indicate that they used controlled groups were 4.4 and 9.0 per 1,000. The blood bank with the 9.0 rate also did not screen for drug addiction. We believe that these rates demonstrate that better screening of donors can help reduce HBsAg positive rates and, consequently, post-transfusion hepatitis.

USE OF HBsAg RATES
TO REGULATE BLOOD BANKS

HEW disagreed with our proposal to establish maximum acceptable incidence rates of positive findings of HBsAg for blood banks because:

--Most cases of post-transfusion hepatitis are non-B and the frequency of HBsAg in a donor population is an unproven predictor of the infectivity of that population.

--It is not clear what constructive measures could be taken by a blood bank that had rates above the maximum.

--Blood banks employing the most sensitive tests would be considered the poorest performers.

--HBsAg rates can only be truly established the first time the population is tested.

--The maximum permissible rate would have to vary from one region to another as does the actual prevalence of HBsAg positivity.

--Blood banks might pre-screen donors before allowing them to donate to achieve low HBsAg rates.

--The cost would be high.

Because HEW believes that HBsAg positive rates are not a proven indicator of the infectivity of the donor population --although studies (see p. 14) have shown a correlation between HBsAg positive rates and post-transfusion hepatitis rates--we agree that establishing such rates to regulate blood banks would present problems. We believe, however, that the HBsAg rates, together with other factors which show a correlation with post-transfusion hepatitis, could be used to schedule inspections of blood banks and, during these inspections, FDA could point out various techniques for improving blood quality. If HEW could establish a good reporting system for post-transfusion hepatitis cases, HBsAg positive rates would diminish in importance as an indicator of the quality of blood because actual cases of hepatitis could be used as the prime indicator for regulating and inspecting blood banks.

HEW's other objections would appear not to apply if HBsAg rates were used as an indicator of the quality of blood for inspection purposes rather than as a firm standard

for regulation purposes. For example, FDA now requires all blood to be tested by one of two available third-generation tests. The sensitivity of the two tests is nearly equal but, if HEW believes the slight variation to be significant, this could apparently be taken into account for the blood banks using the different tests. In addition, HEW could consider HBsAg rates for first-time donors, as well as overall rates, if it believes that this is necessary to determine the relative safety of a donor population. Also, blood banks would be forced to take constructive measures to upgrade their donor population if they knew that actual diagnosed cases of post-transfusion hepatitis were to be used for regulation purposes.

Regarding the cost of operating such a system, we note that many procedures needed already exist, or will exist when a donor registry is operating. All blood is currently required to be tested for HBsAg, and FDA periodically inspects blood banks' operations.

REGULATING BLOOD BANKS BY ELIMINATING PAID BLOOD

HEW disagreed with our proposal (1) to regulate blood banks based upon diagnosed cases of post-transfusion hepatitis caused by the blood collected and (2) to delete from the National Blood Policy the provisions calling for eliminating paid blood. Specifically, HEW contended that:

--Changes from commercial to volunteer blood result in reductions in post-transfusion hepatitis. An 82-percent reduction in post-transfusion hepatitis occurred when the NIH Clinical Center excluded commercial donors and began paying employees to donate.

--Persons knowledgable about hepatitis have not challenged the validity, efficacy, or importance of eliminating commercial blood sources.

--A minor amount of the Nation's blood is commercial blood, but such blood accounts for a major portion of post-transfusion hepatitis cases.

--The vast majority of organizations and individuals associated with blood services in the United States, ranging from donors and collectors, through processors and transfusers, to potential recipients, reject the practice of commerce in blood on health or ethical bases.

--Although blood purchased by hospital blood banks was safer than blood from commercial blood banks, the commercial donors would gravitate to the paid hospital banks if commercial blood banks were eliminated.

--The safest, most feasible cost-effective national policy, and the one with the greatest benefit-to-risk ratio, is excluding paid donors.

We note that commercial blood is collected by blood banks that are proprietary in ownership and not located in hospitals. In addition to paid blood collected by commercial blood banks, much paid blood is collected by some hospital and community blood banks. Overall, this blood is much safer than commercial blood. The National Blood Policy calls for eliminating all paid blood, not just commercial blood as discussed by HEW.

In justifying converting to an all-voluntary system, many of HEW's comments are directed toward the hazards of commercial blood. For example, HEW stated that much evidence has been accumulated showing the high hepatitis risk of blood derived from paid as compared to voluntary donor sources and cited four studies to support the statement. All four studies, however, compared commercial blood--as opposed to paid blood collected by hospital blood banks--to volunteer blood. As shown on pages 7 and 17, paid blood collected by hospitals does not generally pose as great a risk of post-transfusion hepatitis as does paid commercial blood. HEW agrees that some paid blood is less dangerous than some volunteer blood. In addition, the NIH Clinical Center's decrease in the post-transfusion hepatitis rate was the result of converting from a commercial supply of blood to a paid supply, not to a voluntary supply.

HEW's comments show that, on the average, volunteer blood is safer than commercial blood but do not show that volunteer blood is safer than other types of paid blood. In addition, as shown on pages 7 and 17, some commercial blood is safer than volunteer blood. It is clear that not all volunteer blood is safer than all paid blood.

We do not believe that hospital blood banks would generally accept commercial blood bank donors as paid donors if commercial blood banks were eliminated. We developed HBsAg positive rates for seven hospital blood banks that paid donors. Five of these banks said their paid donors consisted of a controlled group. The NIH Clinical Center, for example, paid only employees.

In commenting on the National Blood Policy and the goal of an all-volunteer system, the Mayo Clinic, which pays its donors, informed HEW on April 30, 1974, that:

> "Studies supported by the National Heart and Lung Institute and conducted at the Mayo Clinic between 1966 and 1971 indicated that of every 2,000 units of blood transfused in Rochester, Minnesota, only one was associated with clinical evidence of hepatitis. This is a level of safety that should be sought nationally. During the past 10 years or more, no surgical procedure has been cancelled nor has any patient been deprived of blood at the Mayo Clinic because of an inadequate supply or inability to pay. In this same period of time, over 250,000 units of blood have been collected, processed and transfused at the Mayo Clinic with a loss by outdating of 1-2%. We believe these standards of efficiency, availability and accessibility to be those which should be sought nationally. They may be difficult to attain in every community throughout the United States, but each community should be permitted to strive to attain these goals by whatever means the local community or region considers most desirable. The product, i.e., the degree of success or failure in achieving these goals should be the concern of government, not the means by which it is achieved. The National Blood Policy in determining the methods of attaining the above goals through regionalization (undefined as to size and population), through an all volunteer blood donor system and through alignment of charges and costs for blood services may in some instances, such as ours, produce effects counter to those intended." (Underscoring supplied.)

By a letter dated August 4, 1975, the Chairman of the Clinic's Board of Governors stated that this information was still valid. Thus, not all organizations agree with the National Blood Policy.

The National Blood Policy's stated aims include developing an appropriate ethical climate for the use of human tissues. In this regard, the Policy seeks to end the practice of purchasing blood. It does not, however, preclude special arrangements when very rare blood or blood components are needed and can be obtained only by special consideration for unique donors. Thus, when the situation warrants, compensating donors is still ethical.

HEW officials cited no studies to support its view that excluding paid donors is the most cost-effective national policy. HEW's comments were directed toward the hazards of

commercial blood and the safety of volunteer blood; little evidence was presented to show that all paid blood should be judged in the same light as commercial blood. We do not believe that action should be taken against paid blood banks that can show a valid record of supplying high-quality blood, particularly if such action could jeopardize the adequacy of the blood supply or force a reliance on blood from other sources which is or may be of lesser quality.

BLOOD SUPPLY

HEW predicted that eliminating paid blood would not cause a blood shortage problem and cited a number of areas--including Chicago and the part of the Southwest served by Blood Services, Inc.--that had successfully converted to an all-voluntary system. HEW offered the following points to counter our concern over blood shortages.

--Less than 10 percent of those eligible to donate actually do so, and inducing only an additional 2 percent of the general population to donate by intensified donor recruitment programs would entirely compensate for the loss of commercial blood.

--The loss of high-risk commercial blood could be totally offset by programs which encourage better blood use, such as by decreasing unnecessary single-unit transfusions, using plasma expanders rather than whole blood, using heart-lung machines with smaller priming volumes, using more autotransfusion, and increasing the storage life of banked blood inventories.

--Those donors who are currently paid but are of a socioeconomic class with a relatively low hepatitis risk (i.e., "good" paid donors) are the donors most likely to donate voluntarily when they are adequately informed of the need for donated blood.

Concerning potential blood shortage problems, except for Chicago, our review did not include the areas HEW mentioned as having successfully converted to an all-volunteer system. Our comments about Chicago's problems in meeting its blood needs appear on pages 9 through 11. We repeat that more blood was being shipped into the Chicago area than was being shipped out. HEW did not elaborate on how Chicago was now becoming self-sufficient.

We also reviewed the operations of Blood Services, Inc., in Chicago. Blood Services, a medically sponsored, non-profit corporation headquartered in Arizona, operates a

network of community blood banks, one of which is in Chicago. According to Blood Services officials in Chicago, the shift to an all-voluntary donor system has caused supply problems. During 1972 the Chicago branch collected about 32,800 units of blood from paid and volunteer sources. In 1973, when it switched to an all-voluntary system, only 11,532 units were collected. One official said that since changing to the all-voluntary system there has been no steady supply of blood or components. Before the change, paid donors could be called in to donate in an emergency.

Regarding HEW's three points to counter our concern over blood shortages, we repeat that the National Blood Policy calls for the transition to an all-voluntary blood donation system, which means that all paid blood would be eliminated, not just commercial blood. HEW estimated that 11 percent of the units collected are from commercial donors but did not know how many units of paid blood are collected. Therefore, estimates as to the number of additional donors needed to replace these units or the impact that better blood use would have on offsetting paid units are, in our opinion, highly speculative.

Also, we asked HEW officials (1) how many units of blood could be saved by each of the methods mentioned for better blood use and (2) whether any studies had been performed to show that under an all-volunteer system good paid donors would be more likely to continue to give blood than bad paid donors and to what extent they would continue to donate blood. The officials replied that (1) information was not available as to how many units could be saved by each of the methods for better blood use and (2) they did not know of any studies showing that good paid donors would be more likely to continue to give than bad paid donors.

BLOOD BANK WARNING ABOUT DRUG ADDICTS

Although HEW concurred with our proposal to make known to blood banks our findings about drug addicts donating and selling their blood and stress the importance of not accepting them as blood donors, it raised several points about our review.

According to HEW, it is standard practice to include questions about drug addiction in donor interviews and to select only those who give a negative history and who have no evidence of venipuncture scars suggesting addiction.

Regarding the validity of our questionnaire data, HEW stated that addicts receiving treatment at the drug centers

could have felt pressured to give socially acceptable answers; i.e., that they had donated rather than sold blood or plasma. HEW added that no provision was made for addicts who did not wish to participate in the study and suggested that, if they felt obliged to fill out a questionnaire, the inclination to give socially acceptable answers might be greater, particularly if their answers could be identified with them by center personnel. According to HEW, addicts are notoriously unreliable sources of information, and the accuracy of our information is therefore questionable.

We conducted our review at 31 blood banks, which annually collected a total of 727,284 units of blood. For 14 of these banks, we obtained the questions asked during the donor interviews. The 14 banks had total annual collections of 615,248 units of blood. One blood bank, which collected 6,474 units of blood, asked no questions pertaining to drug addiction and its "Donor Eligibility Guide" made no mention of drug addiction. Five blood banks which collected 498,290 units of blood asked questions pertaining to drugs which we felt were not clearly enough worded to determine if the individual had ever been addicted to drugs. For example, four of these banks asked "Medication or Drugs, Past 6 mos." The other eight banks, which collected 110,484 units of blood, asked questions clearly related to drug addiction or narcotics use.

Regarding checking for evidence of venipuncture scars suggesting addiction, HEW officials agreed that blood bank personnel are sometimes lax, especially if the donor is well dressed.

Concerning the reliability of our data, of 1,321 addicts interviewed that injected drugs, 199 responded that they had donated or attempted to donate their blood or plasma. If they were attempting to give socially acceptable answers, we believe they would have given socially acceptable or unselfish reasons for donating or attempting to donate. Only 20 percent, however, said they donated for unselfish reasons. Most of the remaining addicts said they donated as replacement donors or as prisoners.

In addition, before distributing the questionnaire, we obtained two studies that clearly state that drug addicts' responses are reliable. The first study was performed at the National Institute of Mental Health, Clinical Research Center, Lexington, Kentucky. Based on the verification of information obtained from 100 patients treated under the Narcotic Addict Rehabilitation Act of 1966, the study concluded that researchers need not concern themselves with

the truthfulness of addict informants any more than they would with a less deviant sample.

The other study was performed at the Washington University School of Medicine, St. Louis, Missouri, and was supported by grants from the National Institute of Mental Health. Based on the confirmation of data obtained from 31 individuals who had a public record involving drugs, the study concluded the information obtained from addicts was highly valid.

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In commenting on our report, the American Blood Commission (see app. III) disagreed with our proposals. Its reasons for disagreeing were generally the same as HEW's. It added that, if rates were established for cases of post-transfusion hepatitis, it would be logical to enact legislation prohibiting the transport of blood from an area of the country with a high incidence of hepatitis to one with a lower incidence. The extent and circumstances for transporting blood is, in our opinion, a matter that HEW can consider in regulating the blood supply.

APPENDIX III

THE AD HOC COMMITTEE TO ESTABLISH
THE AMERICAN BLOOD COMMISSION
Suite 608, 1828 L Street, N.W.
Washington, D.C. 20036
AC202 872-1828

July 23, 1975

MEMBER ORGANIZATIONS

American Association of Blood Banks
AFL-CIO
American Heart Association
American Hospital Association
American Medical Association
American National Red Cross
American Society of Clinical Pathologists
Blue Cross Association
Chamber of Commerce of the United States
College of American Pathologists
Council of Community Blood Centers
National Hemophilia Foundation
Pharmaceutical Manufacturers Association

John J. Corson
Chairman
Henry T. Gannon
Professional Associate

Mr. Gregory A. Ahart
Director, Manpower & Welfare Division
441 - G - Street, N.W.
Washington, D.C. - 20548

Dear Greg:

I enclose three copies of the report of a Special Committee created by the American Blood Commission to review the draft report on "Hepatitis Resulting From The Transfusion of Blood" which you made available for our study. I hope you will find this report useful.

The Committee's report was reviewed - in confidence - by the Executive Committee of the American Blood Commission on July 18, and endorsed by that body. The Executive Committee asked me to reaffirm the point made in my letter of June 9 addressed to Mr. Frank D. Etze: This study of a limited and non-random sample of blood banking operations provides no adequate basis for recommending that a national policy (i.e., ..."to eliminate commercialism in the acquisition of whole blood and blood components for transfusion purposes". - National Blood Policy, July 10, 1973) enunciated by the Department of Health, Education, and Welfare and very generally approved by informed personnel throughout the blood service community - donors and consumers as well as the professional personnel operating blood banks be abandoned.

We appreciate this opportunity to study and review this draft report. We further ask that if the report in its present form is submitted to the Congress that this letter and the accompanying report accompany it.

Sincerely,

John J. Corson

JJC/lfd
Encs.

APPENDIX III

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Pharmaceutical Manufacturers Association

John J. Corson
Chairman
Henry T. Gannon
Professional Associate

MEMORANDUM TO: William D. Dolan, M.D.
Herbert F. Polesky, M.D.
Marvin Schneiderman, Ph.D.
Leonard B. Seeff, M.D.
Wolf Szmuness, M.D.

FROM: Tibor J. Greenwalt, M.D.

SUBJECT: Report of Meeting Held July 17, 1975 Relative to GAO Report on "Hepatitis Resulting From The Transfusion of Blood"

An Ad Hoc Committee to review the subject GAO report met in the conference room of the AABB office between 9:30 a.m. and noon on July 17, 1975. The following were present: Tibor J. Greenwalt, M.D., Chairman, William D. Dolan, M.D., Herbert F. Polesky, M.D., Leonard B. Seeff, M.D., Marvin Schneiderman, Ph.D., and Wolf Szmuness, M.D., with Nancy Holland as staff assistant.

The Committee endorses the goal of the GAO report to reduce the incidence of posttransfusion hepatitis. It is apparent to all the members of the Committee that the data were collected by persons who had no previous expertise in the field. It would have been more appropriate to have sought expert advice before starting the project. The protocol for the study should have been prepared with appropriate guidance by experts in the field and necessary supporting disciplines. The status of progress should have been reviewed periodically by these experts to assure that the data were being collected properly and that the conclusions and recommendations would be based on a sound scientific foundation.

RECOMMENDATION #1

Establish for blood banks, maximum acceptable incidence rates of (1) positive findings of HBAg, and (2) actual diagnosed cases of posttransfusion hepatitis resulting from the transfusion of blood collected by particular blood banks.

RECOMMENDATION #2

Periodically review the HBAg positive rates of blood banks and the cases of posttransfusion hepatitis resulting from the transfusion of blood collected by the banks to ensure that they are within the established limits. The extent and priority in scheduling these reviews should be determined based on factors which show a high correlation with posttransfusion hepatitis, such as the percent below poverty level of the donors neighborhood, whether the donors are paid or volunteer, and any other factors identified by HEW.

The recommendations made at the end of Chapter II for the steps to be taken to eliminate high risk donors cannot be fully supported. The premise that elimination of donors who are carriers of the hepatitis B surface antigen will significantly reduce the incidence of posttransfusion hepatitis cannot be upheld by close scientific scrutiny. The Committee agrees that testing for HBsAg must be done and all positive donors must be eliminated from the donor pool. However, there is no scientific evidence that this measure alone has any impact on reducing the rate of posttransfusion hepatitis because of the high incidence of non-A, non-B cases. Dr. Seeff presented evidence supporting this position which has been accumulated over the past five years by carefully coordinated and carefully planned studies conducted by the Veterans Administration.

Since 1969 the VA Hospital, Hines, IL has participated in cooperative studies conducted by the Veterans Administration, related to posttransfusion hepatitis. Patients who received blood transfusions

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were evaluated every two weeks for a minimum of 22 weeks. If hepatitis was suspected (elevation of SGPT and/or bilirubin) the patient was seen at weekly intervals. The passage of the Blood Labeling Act in the State of Illinois required identification of the source of blood as of Oct. 1, 1972. Since July 1, 1973 it has been mandatory to document necessity for the use of paid blood. A summary correlating the incidence of posttransfusion hepatitis and the source of donor blood follows:

PERIOD	Dates	No. Patients	% Paid Blood	% >5 Transfusions	INCIDENCE OF HEPATITIS Icteric	%	Total	%
I	1969-70	217	94.5	12.4	7	3.2	41	18.9
II	1971/9-72	212	97.2	18.4	12	5.8	53	25.7
III	10-72/6-73	77	25.7	23.4	0		6	8.1
IV	7-73/12-74	175	2.6	37.7	2	1.1	12	6.9

In Period I no screening was conducted for HBsAg. In Period II most donor bloods were tested for HBsAg by immunodiffusion or electrophoresis. Period III was a transition between the use of paid and volunteer blood with all bloods tested by Ausria I. During the final period, essentially all blood was from volunteer sources and tested for HBsAg by Ausria I or II. The incidence of hepatitis showed a significant decrease of 68% after conversion to volunteer sources. Results are even more significant as the number of patients receiving greater than 5 transfusions has been steadily increasing (reflecting more cardiac surgery). No significant reduction in posttransfusion hepatitis has been observed at the other participating VA Hospitals where there has been no significant change in the use of commercial donors. The screening of donor blood for HBsAg did not decrease the incidence of posttransfusion hepatitis.

The Committee therefore, feels that this recommendation is not valid.

The availability of more reliable information concerning the rates of posttransfusion hepatitis would be very useful. How-

ever, the Committee does not feel that this information can be used for judging the performance of a blood bank. Such data could be subject to considerable manipulation at the local level and the risk of penalizing those who collect and perform conscientiously presents a real hazard. The fear of possible consequences could readily counteract any benefits to be derived. Nevertheless, it is considered important to establish the feasibility of obtaining this data base. Careful study will be needed to determine whether reporting of all cases of posttransfusion hepatitis by hospitals and individual physicians, required on the national level or mandated by state laws, would be the best approach. Of course, it would also be necessary to assure that proper feedback of this information would occur from the agencies authorized to collect it to the blood banks.

RECOMMENDATION #3

Delete from the National Blood Policy the provision calling for the elimination of the practice of purchasing blood from donors and, in its place, require each blood bank to stay within the limits established for HBAg positives and for cases of hepatitis resulting from the blood they collect.

Under no circumstances can the purchase of blood be condoned.

The NHLI blood resource studies establish that although only approximately 15 percent of the blood for transfusion used in this country is collected by commercial blood banks, this segment causes approximately 45 percent of all the cases of posttransfusion hepatitis. The Committee considers that the most cost-effective way in which to reduce posttransfusion hepatitis by at least 45 percent is therefore the elimination of all paid donors. The fear of causing a shortage of blood is unfounded because it is clear that recruitment of an additional 2 percent of the population would be more than adequate

to close any gap created. Furthermore, the rapid establishment and success of an all-volunteer blood donor program would be badly damaged if any competition for donors would be permitted by payment for blood. There is no question that the incidence of hepatitis would be markedly reduced when payment for blood is completely eliminated. Again, there is no question in general that blood from paid donors is more hazardous than the blood donated by volunteers. It is also unquestioned that selected populations of paid donors can be safer as far as the transmission of hepatitis is concerned than high risk volunteer donors. There is a definite gradation in the incidence of carriers of hepatitis B surface antigen with greater numbers found in the southern part of this country's hemisphere. Establishment of criteria for the establishment of blood banks on the basis of the rate of incidence of hepatitis carriers in the donor population and the rate of posttransfusion hepatitis cases logic were carried one step further, we would have to interdict the collection of blood from any donors in some parts of the country. It would also then be logical to legislate that it should not be permitted to transport blood under any conditions from an area of the country which has a high incidence of hepatitis to one which has a lower incidence of hepatitis.

The Committee felt that before recommending the establishment of a National Federal Registry it would be necessary to carry out a carefully planned feasibility study. The steps recommended by the report cannot be supported. There are serious questions concerning the violation of privacy of information laws. If laws could be passed making reporting compulsory, could they be enforced and would the implementation be feasible and cost-effective? Would the operation of a National Registry be cost-effective?

RECOMMENDATION #4

Make our findings, with respect to drug addicts donating and selling their blood, known to blood banks, and stress the importance of not accepting them as blood donors.

The information in the report concerning drug addicts is not considered to be substantive. No indication has been given as to the proportion of responses out of the total number of questionnaires distributed. Apparently there was no verification of any of the information. Dr. Seeff reported that the VA had collected information on 600 drug addicts. The results were found to be extremely misleading. On attempting to verify the data, many of the donors who claimed to have donated blood turned out to have given under conditions when it was impossible for them to avoid donating, e.g., in the service when there was a great deal of peer pressure, a) first to donate would get weekend passes or b) failure to volunteer might reveal that they were drug abusers.

RECOMMENDATION #5

We recommend that the Secretary, HEW, establish a Federal registry of unacceptable blood donors and periodically disseminate the registry to blood banks for their use. To develop an effective registry system, it will be necessary to:

a) require the reporting of hospitals and doctors of all post-transfusion hepatitis cases.

b) standardize the criteria for classifying a donor as unacceptable,

c) periodically review the operations of the blood banks to ensure that the registry is used in an effective manner, and

d) require blood banks to report all HBAg positive test results.

The Committee also knows that adequate criteria for screening donors with a history of hepatitis or positive tests for hepatitis and for any reason which might make them suspect as possibly hazardous are well established and accepted by all the blood banking agencies in the United States. The authority to enforce these criteria is already vested

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in the Bureau of Biologics of the FDA. It is entirely possible that in visiting any particular blood bank infringements of existing rules, regulations and guidelines may be detected. This is a basic problem faced by all law enforcement agencies.

RECOMMENDATION #6

We recommend that the Secretary of HEW develop a procedure (1) that would require all units of blood to be tested for HBAg by the best test available, and (2) ..... (deleted) ..... designed to assure that in the future new and improved tests are implemented in the shortest time practicable. Factors that should be considered in determining the best test available include effectiveness of the test, cost of performing the test, and availability of materials to perform the test.

[See GAO note.] The recommendation for the use of the best test for hepatitis made in Chapter 4 is considered to be a moot question especially since the publication in the Federal Register of July 15, 1975 (attached) of the requirement by FDA that the most sensitive test for hepatitis must be employed for testing each donation of blood, plasma or serum to be used in preparing a biological product.

RECOMMENDATION #7

We recommend that the Secretary of Health, Education, and Welfare emphasize research:

a) to determine the effects of frozen and fresh washed red cells on post-transfusion hepatitis; and

b) to alleviate the problems currently attributed to frozen blood systems.

GAO note: Attachment is not included in the final report.

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The Committee felt that there is merit to the recommendation in Chapter 5 that it is necessary to conduct further well-controlled studies of frozen, thawed, deglycerolized and washed non-frozen red blood cells to determine whether or not their use will result in a significant reduction in posttransfusion hepatitis. It will also be necessary to establish cost-effectiveness of the use of these products should they prove to merit further consideration.

IN SUMMARY

The Committee unanimously agrees that:

1. Establishment of and periodic review of "acceptable rates" of HBsAg in the donor population of a blood bank will not significantly affect transfusions associated hepatitis.

2. There is need for better reporting and follow-up of case of posttransfusion hepatitis.

3. Elimination of the paid donor is the most cost-effective single measure to effect a significant reduction in transfusion associated hepatitis.

4. Blood banks and blood programs utilizing "voluntary donors" are well aware of the hazard of blood from drug addicts and of the difficulties in relying on the medical histories obtained from such individual.

5. The costs and cost-effectiveness of a registry of unacceptable donors should be determined by a feasibility study --

   a) Requirements for hepatitis reporting already exist and are difficult to enforce.

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b) Adequate standardized criteria for donor acceptability exist and are used by the vast majority of blood banks.

c) Reporting of HBsAg positive donors to local public health authorities in a manner that will insure privacy of the individual is desirable.

6. All units of blood, plasma and serum should be tested by a sensitive, practical, reliable test to demonstrate HBsAg. Funds should be made available to support research to develop sensitive practical ways to eliminate other agents causing transfusion associated hepatitis.

7. Research to determine what effects freezing and/or washing of blood prior to transfusion will have on transfusion associated hepatitis should be supported. The cost-effectiveness and practicality of this approach must be carefully evaluated and may depend on efforts to improve the present state of the art of blood freezing and washing.

8. Studies such as this must have imput from and review by knowledgeable individuals at all stages to insure accurate data is collected and appropriately analysed if meaningful solutions to the problem under study are to be reached.

GAO ANALYSIS OF THE ASSOCIATION BETWEEN HBsAg POSITIVE RATES AND DONOR CHARACTERISTICS

To determine what donor characteristics are most closely associated with a high incidence of HBsAg positive rates, we used a statistical analysis technique called regression analysis. Donor characteristics selected for analysis were (1) whether the donors were paid or volunteer and (2) the socioeconomic conditions of the areas in which the donors live. Our analysis included 21 donor groups--12 paid and 9 volunteer.

PROCEDURE

We developed information on the socioeconomic condition for donor groups for whom blood bank officials knew explicitly the geographical areas in which they lived and for whom blood-screening techniques used were approximately the same. We eliminated blood banks that were drawing blood from a specific segment of the population, such as students or military personnel. Blood bank officials supplied information on where the donors lived and whether they were paid or volunteers. The socioeconomic data was based on 1970 census information. We developed HBsAg positive rates on the basis of blood banks' records. Our analysis should be considered a case study reflecting the situation of the 21 donor groups studied.

We developed data on 11 factors, including the HBsAg positive rate for each donor group. The factors used in our analysis are listed below.

Blood bank factors:

- HBsAg positive rate per 1,000 donors
- Whether donor was paid or volunteer

Socioeconomic factors:

- Percentage black
- Estimated median school years completed
- Percentage of families below poverty level
- Estimated median family income
- Percentage of houses lacking some plumbing
- Percentage of houses lacking complete kitchens
- Estimated median value of house
- Percentage of houses built from 1950 to 1970
- Percentage of houses built before 1940

To examine the relationship between the HBsAg positive rate and the other factors, we performed a number of regression analyses using the HBsAg positive rates as the dependent factor and measuring the effect of the 10 independent factors on the variation in the HBsAg positive rates. These regression analyses were to determine if the fluctuations in the dependent factor were associated with the fluctuations in the independent factor. The statistical significance of the factors which explain the variation of the HBsAg positive rates was tested using the F-test at a 95-percent confidence level. The F-test is a test to determine if the contribution of each factor in the analysis was statistically significant.

In our initial regression analysis we tested all 10 independent factors and found only one statistically significant factor, the percentage of families below the poverty level. Higher percentages of families below the poverty level were associated with higher HBsAg positive rates. In addition, there was a high degree of intercorrelation among the factors used.

To find factors with greater explanatory power, we performed another regression analysis using five independent factors not highly intercorrelated. These factors were (1) whether donor was paid or volunteer, (2) percentage black, (3) estimated median school years completed, (4) percentage of families below poverty level, and (5) estimated median family income. The following table indicates the results.

Regression A

Order of significance	Cumulative R^2	Statistically significant?
Percentage of families below poverty level	.63	Yes
Whether donor was paid or volunteer	.70	Yes
Estimated median family income	.75	Yes

The above three factors appeared at a statistically significant level. The factor specifying the percentage of families below poverty level entered first with an R^2 of .63, implying that it explains 63 percent of the variation in the HBsAg positive rates. The factor on whether the donor was paid or volunteer entered next, yielding a cumulative R^2 of .70, indicating that these two factors together explained only 7 percent more of the variation in the HBsAg positive rate than the poverty level factor alone. The factor on the estimated median family income entered third, yielding a cumulative R^2 of .75. In this regression the

informative on the percentage of families below the poverty level was the best indicator of a higher HBsAg positive rate, explaining 63 percent of the fluctuations in the HBsAg positive rates, while the other two informatives together explain only an additional 12 percent.

We performed two additional regression analyses: one compared the percentage of families below poverty level with HBsAg positive rates and the other compared whether the donors were paid or volunteer with the HBsAg positive rates. The following table indicates the results.

Regression analysis	Factor	R^2	Statistically significant?
B	Percentage of families below poverty level	.63	Yes
C	Whether donor was paid or volunteer	.36	Yes

The results imply that the factor indicating the percent of the families below poverty level explains 63 percent of the variation in the HBsAg positive rates, while the factor indicating whether donors were paid or volunteer when tested alone explains only 36 percent of the variation.

The most important conclusion that can be drawn from our analyses is that the percentage of families below the poverty level is by far the most significant explanatory factor tested. Regression A, which had the best overall statistical properties, clearly demonstrated the superior explanatory power of this factor, which singularly explains 63 percent of the variation in the HBsAg positive rates among our sample, while the factor indicating whether the donors were paid or volunteer singularly explains only 36 percent of the variation.

QUESTIONNAIRE USED AT DRUG TREATMENT CENTERS

1. When did you start injecting (shooting) drugs?

_____
year

2. Since you have been injecting (shooting) drugs, have you ever sold or attempted to sell your blood or plasma?

Yes_____ No_____

(If No go to question 6.)

3. Since you have been injecting (shooting) drugs, were you ever rejected while trying to sell your blood or plasma?

Yes_____ No_____

Reason if rejected:_____

_____

4. If you have sold your blood or plasma since you have been injecting (shooting) drugs:

a. How many times have you sold your blood or plasma?_____

b. When was the last time you sold your blood or plasma?_____

5. Why did you sell or attempt to sell your blood or plasma?

6. Since you have been injecting (shooting) drugs, have you ever donated or attempted to donate your blood or plasma?

Yes_____ No_____

(If No, go to question 10.)

7. Since you have been injecting (shooting) drugs, were you ever rejected while trying to donate your blood or plasma?

Yes_____ No_____

Reason if rejected:_____

_____

8. If you were not rejected since you have been injecting (shooting) drugs:

a. How many times have you donated your blood or plasma?_____

b. When was the last time you donated your blood or plasma?_____

9. Why did you donate or attempt to donate your blood or plasma?

10. Since you have been injecting (shocting) drugs, have you ever had hepatitis?

Yes_____ No_____

(If No, questions are complete.)

11. Since having hepatitis, did you ever sell or donate your blood or plasma?

Yes_____ No_____

If Yes, which one:

sell_____ times sold_____

donate_____ times donated____

APPENDIX VI

PRINCIPAL HEW OFFICIALS

RESPONSIBLE FOR ADMINISTERING ACTIVITIES

DISCUSSED IN THIS REPORT

	Tenure of office	
	From	To
SECRETARY OF HEALTH, EDUCATION, AND WELFARE:		
David Mathews	Aug. 1975	Present
Caspar W. Weinberger	Feb. 1973	Aug. 1975
Frank C. Carlucci (acting)	Jan. 1973	Feb. 1973
Elliot L. Richardson	June 1970	Jan. 1973
ASSISTANT SECRETARY FOR HEALTH (note a):		
Theodore Cooper (note b)	Feb. 1975	Present
Charles C. Edwards	Mar. 1973	Jan. 1975
Richard L. Seggel (acting)	Dec. 1972	Mar. 1973
Merlin K. DuVal, Jr.	July 1971	Dec. 1972
COMMISSIONER, FOOD AND DRUG ADMINISTRATION:		
Alexander M. Schmidt	July 1973	Present
Sherwin Gardner (acting)	Mar. 1973	July 1973
Charles C. Edwards	Feb. 1970	Mar. 1973
DIRECTOR, CENTER FOR DISEASE CONTROL:		
David J. Sencer	Feb. 1966	Present
DIRECTOR, NATIONAL INSTITUTES OF HEALTH:		
Donald S. Fredrickson	July 1975	Present
R. W. Lamont-Havers (acting)	Feb. 1975	July 1975
Robert S. Stone	May 1973	Jan. 1975
John F. Sherman (acting)	Jan. 1973	May 1973
Robert Q. Marston	Sept. 1968	Jan. 1973

[a]Until December 1972 the title of this position was Assistant Secretary (Health and Scientific Affairs).

[b]Acting Assistant Secretary for Health from February to May 1975.