The New England
Journal of Medicine

Volume 310 JANUARY 12, 1984 Number 2

ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) ASSOCIATED WITH TRANSFUSIONS

JAMES W. CURRAN, M.D., DALE N. LAWRENCE, M.D., HAROLD JAFFE, M.D., JONATHAN E. KAPLAN, M.D., LAWRENCE D. ZYLA, M.P.H., MARY CHAMBERLAND, M.D., ROBERT WEINSTEIN, M.D., KUNG-JONG LUI, PH.D., LAWRENCE B. SCHONBERGER, M.D., THOMAS J. SPIRA, M.D., W. JAMES ALEXANDER, M.D., GARY SWINGER, D.V.M., ARTHUR AMMANN, M.D., STEVEN SOLOMON, M.D., DAVID AUERBACH, M.D., DONNA MILDVAN, M.D., RAND STONEBURNER, M.D., JANINE M. JASON, M.D., HARRY W. HAVERKOS, M.D., AND BRUCE L. EVATT, M.D.

Abstract Of 2157 patients with the acquired immunodeficiency syndrome (AIDS) whose cases were reported to the Centers for Disease Control by August 22, 1983, 64 (3 per cent) with AIDS and *Pneumocystis carinii* pneumonia had no recognized risk factors for AIDS. Eighteen of these (28 per cent) had received blood components within five years before the onset of illness. These patients with transfusion-associated AIDS were more likely to be white ($P = 0.00008$) and older ($P = 0.0013$) than other patients with no known risk factors. They had received blood 15 to 57 months (median, 27.5) before the diagnosis of AIDS, from 2 to 48 donors (median, 14). At least one high-risk donor was identified by interview or T-cell–subset analysis in each of the seven cases in which investigation of the donors was complete; five of the six high-risk donors identified during interview also had low T-cell helper/suppressor ratios, and four had generalized lymphadenopathy according to history or examination. These findings strengthen the evidence that AIDS may be transmitted in blood. (N Engl J Med 1984; 310:69-75.)

CASES of the acquired immunodeficiency syndrome (AIDS) were first recognized in homosexual men and in persons who abused drugs intravenously, suggesting a pattern of occurrence similar to that of hepatitis B in the United States.[1-6] Reports of cases of AIDS in men with hemophilia further confirmed this pattern.[7-12] As with hepatitis B, epidemiologic evidence suggests that AIDS is caused by an agent that can be sexually transmitted between homosexual men[13,14] as well as from heterosexual men to their female partners.[15,16] The sharing of contaminated needles is the presumed mode of transmission between drug addicts. The most likely source of transmission of the putative "AIDS agent" to persons with hemophilia is thought to be clotting-factor concentrates (Evatt BL, et al.: unpublished data).[17]

An infant who received multiple transfusions at birth for erythroblastosis fetalis subsequently acquired severe cellular immunodeficiency and multiple opportunistic infections, ultimately dying from *Pneumocystis carinii* pneumonia.[18,19] One of the blood donors was a man who was subsequently diagnosed as having AIDS and who died of it. Other cases of AIDS have been reported to the Centers for Disease Control (CDC) as occurring in persons who did not belong to groups with an increased incidence of AIDS and who had received blood components within five years before the diagnosis of their illness. Below is a summary of these cases and the results of the completed investigations of the blood donors.

From the Centers for Disease Control, Atlanta, Ga.; the Department of Internal Medicine, Michael Reese Hospital, Chicago; the New York City Department of Health, New York; the Beth Israel Medical Center, New York; the Tennessee Department of Public Health, Nashville; the Jefferson County (Alabama) Department of Public Health, Birmingham; and the University of California–San Francisco Medical Center, San Francisco. Address reprint requests to Dr. Curran at the AIDS Program, Centers for Disease Control, Atlanta, GA 30333.

METHODS

Case Definition and Surveillance

The CDC surveillance definition of AIDS includes reliably diagnosed diseases indicative of underlying cellular immunodeficiency in the absence of any other cause of reduced resistance or increased susceptibility to that disease. These illnesses include opportunistic infections such as *P. carinii* pneumonia, Kaposi's sarcoma in persons under 60 years of age, and lymphoma limited to the brain.[20] The retrospective-surveillance methods for AIDS have been described elsewhere.[21] Current reporting is supplemented by active surveillance through city and state health departments as well as investigation of all requests to the CDC for pentamidine isethionate for the treatment of *P. carinii* pneumonia.

Investigation of Patients with a History of Previous Transfusion

Patients with AIDS who did not fit into one of the groups known to have an increased incidence of AIDS were investigated. The medical and social histories obtained included information on receipt of blood or blood products during the five years preceding the diagnosis of AIDS. If no other potential risk factors were identified and the patient had previously received transfusions, he or she was classified as having transfusion-associated AIDS. Detailed information was obtained about the dates and reasons for transfusion and the types of blood products received. With the cooperation of blood-

collection centers, investigators contacted the donors for a personal confidential interview and physical examination and, when possible, to obtain heparinized blood for T-cell–subset analyses and other immunologic studies as previously described.[22] Public-health officials checked the donor names against a list of patients with reported cases of AIDS. Information from the interview was collected before testing, and the interview results were unknown to the technicians. Donors with symptoms or physical findings suggestive of illness were referred to local health facilities. When the results of immunologic studies were abnormal, new specimens were drawn and the studies were repeated. Donors with persistently abnormal immunologic findings were advised to return for further evaluation in three months. An investigation was considered complete when all available donors had been examined and interviewed and the immunologic studies had been completed.

Since all patients with transfusion-associated AIDS had a diagnosis of *P. carinii* pneumonia, their characteristics were compared with those of other patients without known risk factors who were reported to have such pneumonia. Three representative case histories are included from among the completed investigations.

Analyses of Investigations of Donors

If AIDS resulted from transmission of an agent through transfusion, presumably at least one donor would have been affected by the agent in each case. Donors may or may not experience symptoms or have signs associated with AIDS, but most donors transmitting the disease would be expected to come from populations previously recognized as having an increased incidence of AIDS (i.e., homosexual men with multiple partners, abusers of intravenous drugs, persons born in Haiti, or patients with hemophilia). Using the definition of a high-risk donor (a person belonging to a group at increased risk for AIDS or having a reversed ratio [<1.00] of T-helper to T-suppressor lymphocytes), we identified a single high-risk donor during each of the initial investigations, regardless of the number of donors. To test the statistical significance of these findings, we used the binomial model as described below in an analysis of the distributions of high-risk donors in the seven completed investigations.

Analysis of the Distribution of High-Risk Donors in Cases of Transfusion-Associated AIDS

In using the binomial model to analyze the high-risk–donor distributions, we assumed that (1) the seven completed investigations were representative of all cases of transfusion-associated AIDS; (2) the true prevalence of high-risk donors in the overall donor population was no higher than our prevalence estimates (we used the total number of high-risk donors identified in the donor investigations as an estimate of the prevalence of high-risk donors in the overall donor populations); (3) the prevalence estimates could be considered constant for the various cases of transfusion-associated AIDS and the relevant donor populations; and (4) the probability of identifying one high-risk donor was independent of identifying others.

The null hypothesis states that the number of patients with transfusion-associated AIDS exposed to a high-risk donor is not greater than that expected by chance on the basis of the total number of donors to which each patient was exposed and the estimated prevalence of high-risk donors in the overall donor population.

The probability of finding x high-risk donors [f(x)] among an individual patient's set of n donors is determined by using the binomial distribution:

$$f(x) = \frac{n!}{x!\,(n-x)!}\,p^x q^{n-x},$$

where $x = 0,1,2, \ldots n$, p = the prevalence of high-risk donors in the overall donor population, and $q = 1-p$. Hence, the probability of finding no high-risk donors in a set of n donors is

$$f(0) = \frac{n!}{0!\,(n-0)!}\,p^0 q^{n-0} = q^n.$$

The probability of finding one or more high-risk donors in the same set of donors is $1-f(0)$ or $1-q^n$.

Results

By August 22, 1983, 2157 cases of AIDS had been reported to the CDC from the United States. When broken down into mutually exclusive categories, this figure included 2033 persons reported to be either homosexual or bisexual men (71.6 per cent), past or present abusers of intravenous drugs (16.8 per cent), persons born in Haiti and currently living in the United States (5.1 per cent), or persons with hemophilia (0.8 per cent). One hundred twenty-four persons (5.8 per cent) belonged to none of the above high-incidence groups. Of these 124 patients, 82 had a diagnosis of *P. carinii* pneumonia, 23 had opportunistic infections other than *P. carinii* pneumonia, and 19 had Kaposi's sarcoma.

Adequate histories on transfusion were available for 13 of the 19 patients with Kaposi's sarcoma and 22 of the 23 patients with opportunistic infections other than *P. carinii* pneumonia. Of these, only one man with Kaposi's sarcoma had received a transfusion within the previous five years. Since the results of his immunologic tests were normal and his physician considered his course more typical of classic Kaposi's sarcoma, donor investigation was not undertaken and his case was excluded from the analyses.

Of the 82 patients with *P. carinii* pneumonia who were not identified with a high-incidence group, 18 were sexual partners of men or women in high-incidence groups. Of the remaining 64, 18 (28 per cent) gave a history of having received a transfusion within five years before diagnosis and were classified as having transfusion-associated AIDS. Table 1 compares these 18 patients with the remaining 46 patients with *P. carinii* pneumonia who were among persons who were not identified with a high-incidence group. Patients with transfusion-associated AIDS were significantly older and more likely to be white than the other patients with *P. carinii* pneumonia.

Table 2 describes the transfusion histories of the 18 patients with transfusion-associated AIDS. Fifteen of the 18 patients (83 per cent) received transfusions in association with surgery, 9 of whom had cardiac surgery. Although two patients had had mastectomies for breast carcinoma, neither had evidence of persistent or recurrent disease, nor had they received chemotherapy or radiotherapy within one year before the onset of their current illness. The time between transfusion and onset of illness ranged from 10 to 43 months (median, 24.5 months; mean, 22.7), with 15 to 57 months lapsing between transfusion and the diagnosis of *P. carinii* pneumonia (median, 27.5 months; mean, 26.6). The 18 patients received transfusions from as few as 2 to as many as 48 donors (median, 14; mean, 15.9). No single type of blood product was received by all 18 patients: 16 received packed cells, 12 received fresh-frozen plasma, 9 received whole blood, and 8 received platelets.

The first reported case of transfusion-associated AIDS was diagnosed in June 1982, and 12 of the 18

Table 1. Characteristics of Reported Cases of AIDS and *Pneumocystis carinii* Pneumonia in 64 Persons Not Identified as Belonging to a Group at Increased Risk for AIDS.*

	Cases Associated with Transfusion within 5 Years	Cases Not Associated with Transfusion
Number of cases	18	46
Sex		
Male	10 (56)	29 (63)
Female	8 (44)	17 (37)
Ethnic group		
White	16 (89) †	14 (30)
Black	0	18 (39)
Hispanic	1 (6)	13 (28)
American Indian	0	1 (2)
Asian	1 (6)	0
Age (yr)		
Range	19–67 ‡	24–72
Median	54	42
Mean	52.1	41.5
Current status		
Alive	8 (44)	19 (41)
Dead	10 (56)	27 (60)
State of residence		
New York	6 (33)	21 (46)
California	3 (17)	1 (2)
New Jersey	1 (6)	5 (11)
Florida	1 (6)	7 (15)
Other	7 (39)	12 (26)
Year of diagnosis		
Before 1981	0	1 (2)
1981	0	3 (6)
1982	6 (33)	15 (33)
1983 (Jan–Aug)	12 (67)	27 (59)

*Values in parentheses represent rounded-off percentages.

†Patients with transfusion-associated AIDS were significantly more likely to be white than the other 46 patients (chi-square = 15.48; P = 0.00008).

‡Patients with transfusion-associated AIDS were significantly different in age distribution from the other 46 patients (Wilcoxon two-sample test, P = 0.0013).

cases were diagnosed after March 1983. The dates of transfusions were much earlier; 14 patients received transfusions before the first cases of AIDS were reported to the CDC in June 1981.

Donor Investigations

Results of the seven completed donor investigations are summarized in Table 3. Altogether, eight high-risk donors were identified by history or immunologic evaluation. None of the donors identified in this series were reported to have AIDS. Six of the seven patients with AIDS were exposed to at least one donor from a group at increased risk for AIDS, and all seven were exposed to a donor with a decreased helper/suppressor ratio. Five of the six high-risk donors identified by history also had decreased helper/suppressor ratios. The blood components donated by the eight high-risk donors to patients with transfusion-associated AIDS included platelets (three patients), whole blood (two patients), fresh-frozen plasma (two patients), and packed cells (one patient).

The probability that at least the observed number of patients with AIDS had been exposed to one or more high-risk donors by chance alone was 0.014. This probability remained significant when the definition of high-risk donor was changed to include only donors in a group at increased risk of AIDS (P = 0.028) or those with a reversed helper/suppressor ratio (P = 0.007), depending on which definition of high-risk donor was used. Thus, the null hypothesis is rejected, and patients with transfusion-associated AIDS were more likely to be exposed to a high-risk donor than would be expected on the basis of the number of donors to whom each patient was exposed and the prevalence estimates of high-risk donors in the overall donor population.

Among the first 13 cases of transfusion-associated AIDS reported, donor investigations were completed in 7. The blood-donor records for Case 8 were destroyed in a fire. Interviews and examinations of donors have been initiated in three additional cases; a single high-risk donor has been identified thus far in two of these cases.

Selected Case Histories (Also See Table 2)

Case 4

A 19-year-old man had been in good health until he received multiple fractures and a renal contusion in an automobile accident in December 1979. After therapy, including receipt of two units of packed red cells, he was discharged from the hospital on February 21, 1980, and recovered completely from his injuries. In September 1981 he had a thoracic condition (diagnosed as herpes zoster), which resolved shortly. In October 1982 he was hospitalized with respiratory distress, and a bilateral diffuse infiltrate was noted on a chest film. At an open-lung biopsy *P. carinii* was found. The patient responded to therapy with trimethoprim–sulfamethoxazole. He was readmitted on March 7, 1983, for recurrent pneumonia, and *P. carinii* was again isolated. Laboratory studies indicated elevated levels of IgG and IgA in October 1982 and a decreased helper/suppressor ratio (0.7) in March 1983. Despite therapy with trimethoprim–sulfamethoxazole and pentamidine isethionate, he died on March 20, 1983.

The patient had no history of homosexual contact, intravenous drug abuse, or other known or suspected risk factors for AIDS. Although no autopsy was performed, there was no evidence of a concomitant immunosuppressive disease. The two donors were interviewed and examined. One was a healthy married man with no risk factors for AIDS and with normal results on immunologic studies. The second donor, a 32-year-old homosexual man with multiple sexual partners, gave a history of unexplained generalized lymphadenopathy that had persisted since 1979; a lymph-node biopsy specimen demonstrated benign hyperplasia. In April 1983 he had generalized lymphadenopathy and a helper/suppressor ratio of 0.69.

Case 6

A 45-year-old married woman had congenital heart disease that had required a pulmonary valvulotomy in 1957, repair of an atrial septal defect in 1970, and

Table 2. Transfusion Histories of 18 Adults with *P. carinii* Pneumonia and Transfusion-Associated AIDS.

Case No.	Age/Sex; Ethnic Group	Date of Diagnosis of Pneumonia	Date of Tranfusion	Reasons for Transfusion	No. of Units (Type) *	Months from Transfusion to Onset of Illness	Months from Transfusion to Pneumonia Diagnosis	Status of Donor Investigation
1	52/M; white	6/82	3/81	Exploratory laparotomy, peritonitis	4 (2 PC, 2 FFP)	15	15	In progress
2	64/M; Hispanic	7/82	1/81	Cardiac surgery (coronary bypass)	20 (8 PC, 2 FFP, 10 PL)	15	18	Completed
3	56/F; white	8/82	11/77 4/80 †	Mastectomy Hysterectomy	3 (1 PC, 2 WB)	14–43 †	28–57 †	Completed
4	19/M; white	10/82	12/79	Trauma	2 (PC)	34	34	Completed
5	49/F; white	12/82	2/80	Thrombocytopenia	6 (PL)	27	34	Completed
6	45/F; white	12/82	2/79 7/79 6/81 ‡	Cardiac surgery (valvular)	28 (4 PC, 3 FFP, 15 WB, 6?)	10–38 ‡	18–46 ‡	Completed
7	53/M; white	3/83	11/80	Cardiac surgery (coronary bypass)	16 (7 WB, 4 FFP, 5 PL)	26	28	In progress
8	52/F; white	3/83	10/80	Mastectomy	4 (PC)	24	27	Unable to be completed
9	33/F; Asian	4/83	9/81	Cardiac surgery (aortic-valve replacement)	34 (7 PC, 2 WB, 10 FFP, 15 PL)	17	19	Completed
10	62/M; white	4/83	1/82	Vascular surgery (aortofemoral bypass)	31 (6 PC, 18 WB, 7 FFP)	12	15	In progress
11	61/M; white	5/83	12/80	Cardiac surgery (coronary bypass)	23 (5 PC, 8 WB, 7 FFP, 1 PL, 2 Alb)	26	29	In progress
12	55/F; white	5/83	3/80	Cardiac surgery (coronary bypass)	4 (2 PC, 2 FFP)	33	38	In progress
13	66/M; white	5/83	8/81	Cardiac surgery (coronary bypass)	6 (3 PC, 1 WB, 2 FFP)	17	21	Completed
14	60/M; white	6/83	4–6/81 §	Bleeding ulcers	12 (including PC)	24–26 §	24–26 §	In progress
15	67/F; white	7/83	3/80 § 7/81 §	Intestinal polyps Cardiac surgery (aortic-valve replacement)	20 (2 PC, 5 PC, 4 FFP, 9 PL)	18–34 §	24–40 §	In progress
16	44/M; white	6/83	5–6/82 §	Trauma, surgery	48 (7 PC, 20 WB, 2 FFP, 19 PL)	11–12 §	12–13 §	In progress
17	40/M; white	7/83	5/80	Cardiac surgery (coronary bypass)	22 (9 PC, 2 WB, 1 FFP, 10 PL)	37	38	In progress
18	60/F; white	8/83	8/79	Hysterectomy	4 (2 PC, 2?)	39	48	In progress

*PC denotes packed cells, WB whole blood, FFP fresh-frozen plasma, PL platelets, and Alb albumin.

†The later surgery (shorter duration) is considered more likely to be associated with AIDS in this case. One of the two donors for the latter surgery currently has unexplained generalized lymphadenopathy and a persistently reversed helper/suppressor ratio. The shorter duration was used to compute the interval between transfusion and onset or diagnosis.

‡One of the donors during 1981 was a homosexual man with generalized lymphadenopathy and a transiently reversed helper/suppressor ratio. The shorter duration was used to compute the interval between transfusion and onset or diagnosis.

§Because of the absence of complete information, the midpoint between the transfusions was used to compute the intervals between transfusions and onset or diagnosis.

placement of a pacemaker in 1977. She received blood during her procedures in 1957 and 1970, but not in 1977. She remained well until 1979, when she underwent a hysterectomy for benign disease. During that hospitalization, she had hemorrhage and was treated for septic shock and endocarditis. Surgery was required later that year to replace her tricuspid valve. She was hospitalized in July 1981 for replacement of her tricuspid and pulmonic valves and placement of a permanent pacemaker. In April 1982 she was hospitalized for evaluation of unexplained fever. She was discharged without a specific diagnosis or therapy, but was readmitted in August 1982 for persistent fever, dyspnea, diarrhea, unexplained weight loss, and oral candidiasis. In December 1982, a gallium scan of the lungs demonstrated increased radiotracer uptake, chest films revealed progressive diffuse interstitial infiltrates, and *P. carinii* was detected in material obtained by transbronchial biopsy. The results of scalene-node and bone-marrow biopsies were normal. In February 1983 the patient's neurologic status declined. On CT scanning, findings in several areas were compatible with a diagnosis of central-nervous-system toxoplasmosis, although a brain biopsy showed no pathologic process. The indirect fluorescent antibody titer to toxoplasma antigen was 1:128. The patient's neurologic status and CT-scan findings improved after therapy with pyrimethamine, sulfadiazine, dexa-

methasone, and folinic acid, and she was discharged in June 1983. In December 1982 the peripheral-blood white-cell count was 2400 with 9 per cent lymphocytes, and the OKT4/OKT8 ratio was 0.04. In June 1983 she remained leukopenic and lymphopenic (white-cell count, 1700 with 7 per cent lymphocytes). Currently she remains chronically ill.

The patient and her husband of more than 23 years denied having risk factors for AIDS. Although she was hospitalized in a center caring for patients with AIDS, since she had no previously recognized risk factors, this diagnosis was not seriously considered during her first admission.

During her hospitalizations in 1979 and 1981, she received blood components from 28 donors. Nineteen of the 24 American donors were interviewed and examined, and T-cell subsets were analyzed on heparinized blood from 18. Three donors refused testing, one was living outside the United States, and one could not be located. One of the 12 male donors examined was a 28-year-old homosexual man with multiple sexual partners and cervical, axillary, epitrochlear, and inguinal lymphadenopathy noted at the time of examination. His OKT4/OKT8 ratio was 0.8.

Table 3. Prevalence of High-Risk Donors among Donors to Seven Patients with Transfusion-Associated AIDS.

Case No.	All Donors *	High-Risk Donors		
		Belonging to group at high risk for AIDS †	Having T_H/T_S ratio <1.00 †	Other characteristics
2	14 (6)	1 (13)	1 (12)	One man was an asymptomatic former intravenous-drug abuser with a normal T_H/T_S ratio (1.5); a second man had a decreased ratio (0.9) but denied AIDS risk factors
3	3	0 (3)	1 (3)	A man with a persistently decreased T_H/T_S ratio (0.64, 0.71), lymphadenopathy, and a history of syphilis and hepatitis B who denied risk factors for AIDS
4	2	1 (2)	1 (2)	A homosexual man with multiple partners, lymphadenopathy, and a decreased T_H/T_S ratio (0.7)
5	6	1 (6)	1 (6)	A homosexual man with multiple partners, a history of lymphadenopathy, and a currently decreased T_H/T_S ratio (0.54)
6	24 (4)	1 (19)	1 (18)	A homosexual man with multiple partners, lymphadenopathy, and a decreased T_H/T_S ratio (0.8)
9	34	1 (30)	1 (5)	A homosexual man with multiple partners and a decreased T_H/T_S ratio (0.6)
13	6	1 (5)	1 (2)	A homosexual man with multiple partners and a decreased T_H/T_S ratio (0.7)
	89 (10) ‡	6 (78) ‡	7 (48)	

*U.S. donations within five years before diagnosis of AIDS (additional donations obtained from Europe are in parentheses).

†Figures in parentheses indicate number of donors on whom information was available. T_H/T_S denotes T helper/T suppressor.

‡The 78 donors who were interviewed and examined included 52 men and 26 women. Six of the 11 American donors not interviewed were women.

Case 9

A 33-year-old unmarried woman had immigrated to the United States from Hong Kong in 1969. In September 1981 she underwent surgery to replace her aortic valve and received blood products from 34 donors. She remained well until February 1983, when she presented with fever and was found to have acute sinusitis and thrush. In April 1983 she was hospitalized for recurrent fever and cough; a chest film demonstrated bilateral pulmonary infiltrates, and *P. carinii*, *Cryptococcus neoformans*, and cytomegalovirus were found in an open-lung–biopsy specimen. She was profoundly lymphopenic, with a helper/suppressor ratio of 0.75. She denied having sexual contact with members of groups with an increased incidence of AIDS and had no history of intravenous-drug abuse. Thirty of the 34 donors were located and examined, including a healthy homosexual man who had had multiple sexual partners, no abnormalities on physical examination, but a helper/suppressor ratio of 0.60.

Discussion

Epidemiologic data suggest that AIDS is caused by an infectious agent that may be transmitted through sexual contact, through sharing contaminated needles, or through the concentrates used to treat hemophilia. Our description of 18 adults without other risk factors in whom AIDS developed after transfusion indicates that other blood components may transmit AIDS. Furthermore, the seven completed donor investigations provide circumstantial evidence that exposure to as little as one unit may result in transmission. The failure to identify definite cases of AIDS or even severe symptoms among the donors examined suggests that affected donors with only mild or inapparent illness account for the majority of cases of transfusion-associated AIDS.

The clinical and immunologic pattern observed in these 18 adults is essentially identical to that described in other patients with AIDS. These 18 cases represent nearly 30 per cent of the 64 cases of *P. carinii* pneumonia without identified risk factors. In contrast, only 1.5 per cent of the U.S. population receives transfusions each year, although the transfusion rate for persons over 65 is three to four times this figure.[23,24] The 30 per cent proportion associated with transfusion is probably an underestimate since the epidemiologic information is incomplete on many of the remaining 46 patients without a history of transfusions (Table 1). Some of these 46 patients probably had undetected

risk factors, since many died before adequate histories were obtained.

Over 60 per cent of cases of transfusion-associated AIDS were reported from New York, California, New Jersey, and Florida — the four states with the largest number of reported cases of AIDS. This is consistent with the observation that most blood used for transfusion is obtained in the region in which it is used.

The profiles of the patients with transfusion-associated AIDS closely resemble those of other recipients of transfusions in the United States, although they were older and more likely to be female than other groups with AIDS. Nearly 40 per cent were 60 years of age or older. In 1980, 57 per cent of the more than 3 million transfusion recipients in the United States were women, and the 11 per cent of the population over 65 years of age accounted for 44 per cent of the transfusion recipients.[24] Patients with AIDS had most often received their transfusions in association with surgical procedures, often coronary-bypass surgery, or for other conditions not known to be associated with severe clinical immunosuppression. In comparison, 62 per cent of the transfusions in the United States are associated with surgical procedures, with malignant neoplasms and cardiovascular disorders the two most common disease categories listed for transfusion recipients.[24]

All 18 patients with transfusion-associated AIDS had a diagnosis of *P. carinii* pneumonia, the most common serious opportunistic infection among other groups of patients with AIDS. Since the surveillance definition of AIDS excluded cases of Kaposi's sarcoma in persons over 60 years of age, a reported case of disseminated Kaposi's sarcoma associated with transfusion in a 69-year-old man was not included above. When the sarcoma was diagnosed in late 1982, the patient's immunologic test results and rapidly fatal course were more typical of the Kaposi's sarcoma seen in AIDS than of the classic form of the disease seen in elderly men. Sixteen months before the onset of symptoms the patient had received three units of blood during coronary-bypass surgery. One of the two donors who were located and examined was a homosexual man with multiple sexual partners, a recent history of zoster, and an OKT4/OKT8 ratio of 1.1.

The mean number of units received by patients with transfusion-associated AIDS (16) was five times greater than the slightly more than three units per patient reported in national surveys of transfusions.[23,24] Receipt of a larger number of units would increase one's risk of exposure to a rare agent, but there may be additional factors related to multiple transfusions.

The finding of a suspect donor associated with each case of transfusion-associated AIDS was unlikely to have occurred by chance. Only 6 of 78 donors interviewed were identified as belonging to groups with an increased incidence of AIDS, and these 6 men accounted for 5 of the 7 with decreased helper/suppressor ratios. The validity of the use of the binomial model to analyze the distribution of high-risk donors in the completed investigations required certain assumptions to be valid. The representative cases investigated involved no known selection bias. Although all unknown bias cannot be ruled out, the prevalence estimates used in the analyses were conservative. The true prevalence of homosexual men with multiple partners and of past or present abusers of intravenous drugs in the donor population is unlikely to exceed the 8 per cent estimate substantially. The 15 per cent prevalence estimate for decreased helper/suppressor ratios is very conservative, since it is six times greater than normal control values in the CDC laboratory.

Investigation of transfusion-associated cases may provide insight into the natural history of AIDS. The mean period between transfusion and diagnosis (27 months) in the cases of transfusion-associated AIDS was even longer than that noted in a cluster of sexually linked cases among homosexual men.[14,25] Four of the high-risk donors were noted to have generalized lymphadenopathy, a condition often associated with AIDS. The donors themselves were often unaware of the lymphadenopathy, which was sometimes documented months to years after donation. Compliance with current guidelines for prevention of AIDS would now result in the exclusion from donating blood of the five homosexual men with multiple partners and the man with a history of drug abuse.[26]

The pattern observed in the investigation of transfusion-associated AIDS in adults is consistent with the case of acquired immunodeficiency after transfusion in an infant.[18,19] Additional cases of unexplained immunodeficiency and severe opportunistic infections have been reported in infants.[27-29] Of 28 infants whose cases were reported to the CDC, 17 were born to parents who belonged to a group with an increased incidence of AIDS. Two of these 17 infants and 6 of the other 11 infants had received transfusions shortly after birth. Further investigation of these cases and of the pediatric acquired immunodeficiency syndrome are needed to clarify the meaning of transfusion-associated disease in infants.

The current number of cases of AIDS associated with transfusion is small, representing about 1 per cent of the reported cases of AIDS in the United States. These 18 cases were diagnosed during approximately 12 months, a period when over 3 million persons in the United States received transfusions. However, most of these patients received their transfusions between 1979 and early 1982, a time when the prevalence of AIDS — and presumably of donors affected by the putative AIDS agent — was much lower than during late 1982 and early 1983.

In March 1983 the Public Health Service recommended that persons with symptoms suggestive of AIDS and members of groups at increased risk for AIDS refrain from donating blood or plasma.[26] Several other organizations, including the American Red Cross, the American Association of Blood Banks, the National Hemophilia Foundation, the American Association of Physicians for Human Rights, and the

Council of Community Blood Centers, have issued similar recommendations, and the Food and Drug Administration has issued specific guidelines for blood- and plasma-collection centers. Although it will not be possible to evaluate the effectiveness of these measures immediately, compliance with them should decrease the number of blood donations potentially associated with the transmission of AIDS.

Note added in proof: By December 12, 1983, 2952 cases of AIDS had been reported to the CDC. Among these, 31 adults are under investigation as having received blood transfusions within five years before diagnosis and having no other identified risk factors.

We are indebted to the following people for assisting in the evaluation and investigation of cases and donors: Pauline Thomas, M.D., Stephen Friedman, M.D., Meredith Smith, James Monroe, Rebecca Reiss, and Armondo Hermoso, M.D., New York City Department of Health; Johannah Pindyck, M.D., New York Blood Center; Shelley Gordon, M.D., and Robert Holtzman, M.D., Bellevue Hospital, New York; Carol Harris, M.D., and Neil Steigbigel, M.D., Montefiore Medical Center, New York; Donald Kaminsky, M.D., and Patricia Wexler, M.D., Beth Israel Medical Center, New York; Selma Dritz, M.D., San Francisco Department of Health; Stanley Deresinski, M.D., and Richard Miller, M.D., Stanford University Medical Center; Herbert Perkins, M.D., Irwin Memorial Blood Bank, San Francisco; Toby Kircher, M.D., Connecticut Department of Health; Joseph Lossick, D.O., Columbus (Ohio) Department of Health; Robert Thompson, M.D., University of Virginia Medical Center; Leroy Harris, M.D., University of Alabama Medical Center, Huntsville, Ala.; Robert C. Rendtorff, M.D., Memphis–Shelby County Health Department; Emmel Golden, Jr., M.D., and William Potter, M.D., Baptist Memorial Hospital, Memphis, Tenn.; Armando Orlina, M.D., Antonio Chan, M.D., Mark Levin, M.D., and Sherwin Kabins, M.D., Michael Reese Medical Center, Chicago; and Kenneth Debeneditis, M.D., Redding Hospital Medical Center, Redding, Pa.; to Lewellys Barker, M.D., Joseph Bove, M.D., George Grady, M.D., Martin Hirsch, M.D., Leon Hoyer, M.D., and Cladd Stevens, M.D., for reviewing the cases and the manuscript; to Frances Porcher and Walter Dowdle, Ph.D., for editorial assistance; and to Quo Vadis Harris for help in preparing the manuscript.

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