Methodologic Approaches to Surveillance of HIV Infection Among Blood Donors

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The HIV Blood Donor Study Group is made up of officials of participating blood donor center organizations who contributed to planning the survey and to the preparation of this paper. A list of the members of the group, and their organizations, is shown separately.

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Synopsis

Blood donors make up the largest group in the United States that is tested for human immunodeficiency virus, type 1 (HIV) antibody. The blood donor population is ideal for detecting and quantifying uncommon or unrecognized modes of HIV transmission in the general population because persons at known risk for HIV infection are excluded from donating blood.

The national HIV surveillance program consists of a centralized computer database of information on all donations at selected American Red Cross blood centers, which together account for about a quarter of the blood supply, and all donations at 20 regional blood centers where seropositive blood donors are interviewed to evaluate their risk factors for HIV infection and to determine their epidemiologic characteristics and motives for donation.

Trends in HIV prevalence and incidence within specific demographic subgroups are determined for first-time and repeat donors. Combining the trends with HIV-risk profile data from seropositive donors provides a rate for HIV seropositive donors with no identified risk. Epidemiologic and behavioral data from seropositive donors will help in the development and evaluation of future donor deferral strategies.

A COMPLEMENTARY FAMILY of surveys and studies has been organized by the Public Health Service's Centers for Disease Control (CDC) to provide empirical estimates of the extent of the human immunodeficiency virus, type 1 (HIV) epidemic in the United States (*1*).

When the surveys and studies are analyzed together, and their limitations and biases taken into account, it will be possible to describe and monitor the levels and trends of HIV infection in different population groups.

Blood donors are the largest population group screened for HIV antibody in the United States. However, levels and trends of HIV prevalence among blood donors may not reflect those of the general population, because persons at risk for HIV infection are actively discouraged from donating blood. HIV surveillance of blood donors remains important because of the self-deferral of high-risk donors and the large number of persons tested. These factors make blood donors an ideal population for detecting and quantifying less frequent modes of HIV transmission. Furthermore, repeat donors are screened for HIV antibody each time they donate, making them one of the few large populations in which the incidence of HIV infection can be directly measured (*2, 3*).

We describe how persons at risk for HIV are excluded from donating blood, as well as the HIV antibody screening of blood donors, and the national blood donor HIV surveillance system.

Characteristics of Blood Donors

About 8 million people donate blood about 12 million times a year (*4*), and perhaps half of all Americans have donated (*5*). Those who donate are more likely to be male, white, between the ages of 20 and 40 years, and to have higher incomes and educational status than those who do not (*6*). Although donors may give blood every 8 weeks, the average donor does so every 7 to 8 months. About 16 percent of donations come from first-time donors, half of whom are male; the remaining donations are collected from repeat donors, of whom 60 percent are male. These differences may reflect a greater tendency for female donors to give only once or to donate less frequently. Most people donate for

Criteria Used by the American Red Cross to Exclude Persons at High Risk for HIV Infection from Donating Blood[1]

Man who has had sex with another man since 1977

Persons who have ever used illegal drugs by needle

Immigrants or visitors from Haiti, sub-Saharan Africa, islands close to sub-Saharan Africa, or West Africa, who have entered the United States since 1977

Persons who have visited those areas since 1977 and who received a blood transfusion in those areas or have had sex with persons from those areas

Persons with signs or symptoms of AIDS (listed in information pamphlet given to prospective donors)

Persons who have ever had a positive test for HIV antibody

Persons with hemophilia who have received clotting factor concentrates since 1977

Persons who are or have been the sex partners of any person described above since 1977

Men or women who are now or have been prostitutes since 1977

Heterosexual sex partners of male or female prostitutes within the last 6 months

[1] Similar criteria apply for blood centers other than those of the American Red Cross.

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homologous transfusion, in which blood products are infused into another person. However, those donating for autologous transfusion, for later infusion into the donor, are a small but increasing proportion of all donors, amounting to 1.0 percent in 1987, and 1.6 percent in 1988 (unpublished data, American Red Cross, Dodd, September 1989).

Since 1983, CDC has recommended that persons who are at risk for acquired immunodeficiency syndrome (AIDS) not donate blood (*7*). Although an estimated 34 to 41 percent of men and 42 to 45 percent of women are ineligible to donate blood according to American Red Cross criteria, only an estimated 14 to 19 percent of men and 2 percent of women are ineligible because of HIV risk factors (*8*). Criteria used by the American Red Cross to exclude those at high risk for HIV infection from donating blood are shown in an accompanying box.

Blood Donor Screening

Most persons providing blood for transfusion in the United States are not paid. In addition to the special efforts to discourage those at high risk for HIV infection from donating blood, some with HIV risk may be screened out for other reasons. For example, those with a history of jaundice or hepatitis, or with serologic markers of hepatitis infection, are deferred from donating blood. Because intravenous drug use and male homosexuality are risk factors both for HIV and hepatitis, those deferred because of possible exposure to hepatitis also may be more likely than other blood donors to have HIV infection. Of 12 HIV-seropositive repeat donors in Los Angeles, in whom seroconversion was documented or whose donations were known to transmit HIV infection, 3 (25 percent) had hepatitis B core antibody; 2 of the 3 were homosexual men (*9*).

The Food and Drug Administration (FDA) requires that several procedures be incorporated into donor screening specifically to discourage those at increased risk for HIV infection from donating blood. These include asking questions about AIDS-related symptoms, sexual contact with persons who have AIDS or with persons at risk for HIV infection, travel outside the United States, and history of drug abuse. FDA requires that donors be able to designate confidentially that a blood unit should not be used for transfusion. In addition to these requirements, blood banking organizations and the public health community have instituted media campaigns and other measures to increase public awareness of the fact that persons at risk for HIV infection should not donate blood.

Typically, a prospective donor at blood collection sites is given information that describes the risk factors for HIV infection and discourages anyone at high risk from donating. A nurse then asks about drug injection history, travel outside the United States, and medical symptoms, including those suggesting HIV infection. A donor registration form that gathers information about previous blood donation, physical symptoms, recent travel, and risk factors for HIV infection is completed and reviewed by a nurse or a technician who determines whether the prospective donor may donate. Finally, the prospective donor reads a card that explains HIV risk factors and places one of two coded labels on the card, indicating whether the blood should or should not be used for transfusion, a method called confidential unit exclusion. Donors are given a telephone number to call

if they later decide that their blood unit should not be used for transfusion.

The deferral process is fairly standard in all blood centers; however, criteria for donor exclusion, information given to prospective donors, and the methods for interviewing prospective donors about HIV risk factors differ somewhat among blood centers other than those associated with the American Red Cross.

HIV Antibody Testing in Blood Centers

Since mid-1985 all blood for homologous transfusion has been tested for HIV antibody (*10*). Blood samples are tested by an enzyme immunosorbent assay (EIA), and repeatedly reactive specimens are tested by Western blot. Blood repeatedly found to be reactive by EIA is discarded. A few blood centers do not transfuse blood that is initially reactive by EIA, regardless of repeat EIA and Western blot results. Blood centers may use different criteria for a positive Western blot that may affect who is notified of seropositive status and the reported seroprevalence rate.

The only FDA-licensed Western blot test requires that antibody to the HIV proteins p24, p31, and either gp41 or gp120/gp160, be considered positive. The American Red Cross criteria require the presence of antibodies to at least one gene product from each of *env* (gp41, gp120/gp160), *pol* (p31, p66/51), and *gag* (p17, p24, and p55) genes. Donors are not notified of the test results if their blood has antibody to some HIV proteins but does not meet the criteria for a positive Western blot test.

Blood Donor HIV Surveillance System

General description. The national surveillance system determines levels and trends of HIV antibody for all donors in approximately half of the 56 American Red Cross blood centers and evaluates HIV risk factors, epidemiologic characteristics, and motives for donation of seropositive donors at 20 blood centers. The system to determine levels and trends of HIV antibody has a computer database at American Red Cross headquarters that contains demographic, donation history, and laboratory information for each donor at participating blood centers. The data base information variables are shown in an accompanying box. This database is updated quarterly from information routinely stored in each blood center's computer records. Only American Red Cross blood centers are included in this study because their uniform blood donor screening procedures ensure comparability of data and because most use one of two computer systems, minimizing software development for central data collection. In addition, the American Red Cross is the largest blood banking organization in the United States (the American Red Cross serves approximately 50 percent of the U.S. population, or 124 million people). Among surveillance systems for HIV infection, only the National Survey of Childbearing Women (*1*) and the Military Recruit Applicant HIV Screening Program (*11, 12*) data bases have broader geographic representation.

American Red Cross Database Variables

Donation characteristics
American Red Cross region
First-time donor (at American Red Cross)
Donor type (regular, directed, or autologous)
Self-excluded (confidential unit exclusion)
Date of current donation
Date of previous donation

Donor characteristics
Gender
Birth date
Zip code of residence
State of residence of donor
Race or ethnicity (gathered only at some centers)
History of blood transfusion

Laboratory test results
HIV enzyme immunoassay (EIA)
HIV Western blot
Alanine aminotransferase (ALT) (non-A, non-B hepatitis screening)
Hepatitis B core antibody (anti-HBc) (non-A, non-B hepatitis screening)
Hepatitis B surface antigen (HBsAG)
VDRL (serologic test for syphilis)

Blood centers in both high and low AIDS-incidence areas participate in the study of seropositive blood donors because the epidemiologic characteristics of seropositive donors may vary geographically. At each participating blood center, a trained interviewer administers a standardized questionnaire to each consenting seropositive donor, usually at the time of notifying the donor of seropositive status. The interview covers HIV risk factors and surrogates of high-risk behavior, such as a history of sexually transmitted diseases, as well as other possible means of HIV acquisition. If consent is given, sex partners of seropositive donors without identified risk are interviewed and offered HIV antibody testing. If the interview of a seropositive donor suggests unusual modes of transmission, such as household transmission, a detailed investigation by local or State health department or CDC officials may be initiated.

Seropositive donors who at the interview do not acknowledge HIV risk factors that would have dis-

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'As part of the national HIV surveillance system, levels and trends of HIV antibody are determined for all donors at about half of the 56 American Red Cross blood centers.'

qualified them from donating blood are classified as having no identified risk (NIR). They may have acquired HIV heterosexually from a person who also acquired HIV heterosexually, reflecting the so-called secondary wave of heterosexual transmission, or by some other uncommon route, such as percutanous exposure in a health care setting. The HIV prevalence of those identified as NIR, determined by multiplying the proportion of seropositive donors who have no identified risk by the proportion of all donors who are seropositive, should reflect the levels and trends in HIV transmission occurring by uncommon means in the general population. HIV prevalences among NIR persons are computed within specific demographic subgroups for first-time and repeat donors. For prevalence calculations, donor population denominators are obtained from the central computer database for American Red Cross centers or are independently compiled for centers outside the American Red Cross.

Method for calculating prevalence and incidence. The HIV antibody seroprevalence from April 1985 through September 1988 among American Red Cross first-time donors was 0.039 percent (0.063 percent for men and 0.014 percent for women). The prevalence for first-time donors was higher than for repeat donors, which was 0.012 percent (0.018 percent for men and 0.003 percent for women). The lower seroprevalence in repeat donors is largely due to the fact that seropositive donors are not allowed to donate again and have been gradually screened out of the donor pool since HIV screening began in 1985.

Currently identified seropositive repeat donors must have seroconverted since their previous donation (if the previous donation occurred after HIV screening began in 1985), whereas seropositive first-time donors could have seroconverted at any time since the HIV epidemic began. Therefore, HIV antibody prevalence in first-time blood donors, or those not previously screened for HIV antibody in the blood donation setting, may more accurately reflect HIV prevalence among persons at low risk in the general population. Correspondingly, HIV incidence in previously tested repeat donors may reflect incidence trends for persons at low risk in the general population.

Calculating the incidence of HIV infection in repeat donors is complicated by the fact that repeat donors wait varying lengths of time between donations and because additional donors are continuously entering the repeat donor pool, while others stop donating. The computer database at American Red Cross national headquarters is organized so that there is one record for each donation. Each record contains the dates of the current donation and the most recent previous donation, but because each record does not contain a unique donor identifier, it is impossible to link two or more records to a single donor.

The following formula can be used to calculate inci-

dence (in person-months of observation) within a defined period (P) after HIV antibody testing began in 1985.

$$\text{Incidence} = \frac{N_{sp}}{\sum_{i=1}^{N} (T_c - T_d)_i}$$

where

N_{sp} = the number of seropositive donors with at least two donations in period P (documented seroconversion in period P)

N = the number of donations in period P when the date of the most recent previous donation also was in period P

T_c = the month of donation, and

T_d = the month of most recent previous donation

Bias can be introduced with this method of calculating incidence when the time period P is relatively short, such as 1 year. To be included in this computation of incidence, a donor has to donate twice within period P, thus systematically excluding donors who donate at time intervals longer than P.

If donors who donate infrequently are different with respect to HIV risk from those who donate frequently, bias would be introduced.

Interpretation of data. One limitation of the American Red Cross computer database is that some important blood centers, such as those in New York City and San Francisco, are not included. The study of seropositive donors also has limitations. First, some seropositive donors cannot be interviewed because they move or give fictitious addresses; others can be located but will not agree to be interviewed. The resulting nonresponse biases are difficult to determine. Among those who consent to an interview but do not acknowledge HIV risk factors, it is sometimes difficult to ascertain whether the donor chooses not to report a known HIV risk behavior, is not aware that he or she has been at risk (such as a woman who had no knowledge that her heterosexual partner was bisexual or was an intravenous drug user), or more rarely, has a false-positive test result. Because these factors can misclassify persons into the no identified risk group, this study will always overestimate the true rate of those without identified risk.

Confidentiality. The American Red Cross computer database does not contain personal identifiers. The study of seropositive donors uses code numbers so that personal identifying information is not transmitted to CDC. Blood centers routinely maintain a confidential file of the names of seropositive donors in a donor-exclusion file in case the donor attempts to donate again.

Application of Data

The surveillance systems are now providing data on the levels (that is, the prevalence and incidence) and trends of HIV infection in low-risk groups of the general population. In addition, the detailed data on the epidemiologic characteristics of seropositive donors and their motives for donating are essential for developing and evaluating future donor deferral strategies.

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