HIV Seroprevalence Surveys of Childbearing Women—Objectives, Methods, and Uses of the Data

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Synopsis

A seroprevalence survey of human immunodeficiency virus (HIV) among childbearing women is being conducted in 43 States and Territories as one of the family of HIV seroprevalence surveys. This blinded survey, in which serologic test results are not linked to identifiable persons, uses neonatal dried blood specimens on filter paper to test for maternal antibodies to HIV. This survey provides relatively unbiased estimates of prevalence of HIV infection in the population of women delivering live children during given survey periods, by month or quarter of delivery, geographic area, and demographic subgroup.

This objective will be met while protecting the integrity and efficient conduct of neonatal screening programs and ensuring patient anonymity. Information from this survey will be used to (a) *assess the levels and trends of HIV infection in women and infants,* (b) *help develop and evaluate prevention programs, and* (c) *project the number of women and children who will develop HIV infection and the acquired immunodeficiency syndrome (AIDS) and will require health care and social services in the future.*

EPIDEMIOLOGIC SURVEILLANCE of human immunodeficiency virus type 1 (HIV 1) infection in women of reproductive age is of public health importance because sexually active women are at risk of exposure to HIV through intravenous (IV) drug use or through heterosexual transmission, particularly as sex partners of IV drug users. In addition, infected women can pass the infection to their offspring. As of July 1, 1989, a total of 8,727 women with acquired immunodeficiency syndrome (AIDS) were reported to the Centers for Disease Control (CDC) (*1*); of these, 3,449 (40 percent) were reported from July 1988 through June 1989 alone. Of women reported during 1988–89, 1,772 (51 percent) used IV drugs, 1,040 (30 percent) had heterosexual contact with a person infected with HIV or at increased risk of exposure, and 305 (9 percent) had no identified risk of exposure. Of the 1,681 pediatric cases of AIDS (patients under 13 years of age at diagnosis), reported from 1981 through June 1989, 1,334 (79 percent) had become infected through perinatal exposure (*1*).

Because of the lengthy incubation period between infection and onset of clinical AIDS, however; AIDS case surveillance does not necessarily reflect current patterns and trends of HIV infection among women or newborns. Obtaining estimates of the prevalence of HIV infection among women of reproductive age, by demographic subgroup and geographic area, is important to ascertain the current extent of infection. By monitoring trends of HIV prevalence over time, changes in prevalence and in the dynamics of the epidemic can be detected relatively early. This information will be vital to State and local health departments to develop and direct effective education and prevention materials and family planning services, to evaluate the effect of education and prevention activities on virus transmission, and to plan the health care and social

Table 1. Percent distribution of 3,701,000 women delivering a child in the preceding 12 months (CPY) and 52,139,000 women of reproductive age (WRA, 18–44 years), by age and racial and ethnic group[1], United States, 1985

	Percentage of total populations							
	White		Black		Hispanic		Total	
Age group	CPY	WRA	CPY	WRA	CPY	WRA	CPY	WRA
18–24 years	24.2	20.2	7.0	3.6	3.9	2.3	35.1	26.1
25–29 years	26.7	16.6	3.5	2.7	3.3	1.8	33.5	21.1
30–34 years	16.8	16.2	2.1	2.5	2.3	1.5	21.2	20.2
35–39 years	6.7	14.5	1.2	2.1	0.7	1.2	8.6	17.8
40–44 years	1.0	12.3	0.2	1.5	0.2	1.1	1.4	14.9
Total	75.4	79.8	14.0	12.4	10.4	7.9	100	100

[1]Distributions differ, chi square $P < 0.001$.
SOURCE: Reference *25*.

Table 2. Percent distribution of 3,701,000 women delivering a child in the preceding 12 months (CPY) and 52, 139,000 women of reproductive age (WRA, 18–44 years), by income and racial and ethnic group[1] United States, 1985

	Percentage of total populations							
	White		Black		Hispanic		Total	
Income (U.S. dollars in thousands)	CPY	WRA	CPY	WRA	CPY	WRA	CPY	WRA
Less than $10.0	12.0	10.0	6.5	4.4	4.3	2.3	22.8	16.7
$10.0–$14.9	8.9	7.6	2.0	1.8	1.7	1.3	12.6	10.7
$15.0–$24.9	15.9	15.6	2.4	2.5	2.2	1.7	20.5	19.8
$25.0–$34.9	15.1	15.3	1.7	1.5	1.1	1.2	17.9	18.0
$35.0 or more	21.2	28.4	1.3	1.8	0.8	1.2	23.3	31.4
Not reported	2.3	2.7	0.2	0.4	0.4	0.2	2.9	3.3
Total	75.4	79.6	14.1	12.4	10.5	7.9	100	100

[1]Distributions differ, chi square $P < 0.001$.
SOURCE: reference *25*.

services required by women and children with HIV infection and AIDS.

In 1987–88, CDC, in collaboration with State and local health departments, developed and implemented the family of HIV seroprevalence surveys, a comprehensive, national, sentinel surveillance system for HIV (*2–9*). As part of this HIV surveillance system, CDC, in collaboration with the National Institute of Child Health and Human Development (NICHD) and State health departments, developed a protocol that outlines standardized survey methods and laboratory testing procedures to be used by participating States and Territories to conduct HIV seroprevalence surveys among childbearing women. The protocol incorporated features from earlier surveys designed and conducted by the Massachusetts Department of Public Health (*10*) and the New York State Health Department (*11*).

Investigators at the Massachusetts Department of Public Health recognized that because maternal antibodies are passively transferred across the placenta (*12, 13*), blood specimens routinely collected from neonates just after birth for metabolic screening could be tested for maternal antibodies to HIV. Thus, it has been technically possible to conduct an HIV seroprevalence survey of women delivering live children by testing the excess dried blood spot specimens that remain after metabolic screening. Moreover, because specimens for neonatal screening generally are received, processed, and tested at central laboratories, a representative sample of these specimens can be obtained for testing.

Objectives

As of 1989, 43 States and Territories have completed, are conducting, or are planning to conduct their first annual survey of childbearing women by testing neonatal blood specimens for HIV antibodies. The objective of these surveys is to provide estimates of the

Table 3. Percent distribution of 3,701,000 women delivering a child in the preceding 12 months (CPY) and 52,139,000 women of reproductive age (WRA, 18–44 years), by metropolitan residence and racial and ethnic group[1], United States, 1985

	Percentage of total populations							
	White		Black		Hispanic		Total	
Area of residence	CPY	WRA	CPY	WRA	CPY	WRA	CPY	WRA
Central metropolitan	22.4	22.6	8.0	7.1	6.1	4.4	36.5	34.1
Suburbs, metropolitan	37.7	40.4	3.6	3.2	3.5	2.8	44.8	46.4
Nonmetropolitan	15.4	16.8	2.5	2.0	0.8	0.6	18.7	19.4
Total	75.5	79.8	14.1	12.3	10.4	7.8	100	100

[1]Distributions differ, chi square $P < 0.001$.
SOURCE: Reference 25.

prevalence and trends of HIV infection in the population of childbearing women throughout the United States, by demographic and local geographic subgroups. This objective must be met while ensuring the integrity and efficient conduct of established neonatal screening programs and the absolute anonymity of individuals.

Characteristics of Surveyed Population

In 1984, 99.0 percent of all babies born in the United States were delivered in hospitals (*14*). Compared with the subset of women of reproductive age 18–44 years, for whom there are recent data available, a higher proportion of women delivering children are from the younger age group of 18–29 years (68.6 percent versus 47.2 percent $P < 0.001$; table 1), are black and Hispanic (24.4 percent versus 20.3 percent, $P < 0.001$; table 1), from households with incomes of less than $15,000 per year (35.4 percent versus 27.4 percent, $P < 0.001$; table 2), and live in central metropolitan areas (36.5 percent versus 34.1 percent, $P < 0.001$; table 3).

Neonatal Screening for Metabolic Disorders

At least 90 percent of newborns in U.S. hospitals are screened for relatively rare metabolic disorders, including phenylketonuria and congenital hypothyroidism. Prompt treatment of identified disorders allows affected infants to develop without the mental retardation otherwise caused by the disorder. Because of the efficacy of therapeutic interventions, neonatal screening is mandated by law in 49 of the 50 States, the District of Columbia, and Puerto Rico (*15*).

Survey Methods

A standard survey design (with options for local variation) adopted for use in 38 States, the District of Columbia, and Puerto Rico links the mother's demographic or residential information or hospital geographic location, or both, to each tested specimen. In three States, demographic and geographic information is not retained. As a requirement of the survey, personal identifying information is removed before testing so that serologic test results cannot be linked to identifiable persons. Such a blinded, unlinked approach obviates the need for informed consent, thereby eliminating the self-selection bias in most voluntary (nonblinded) HIV seroprevalence surveys.

Table 4. Testing for change in seroprevalence between two time periods[1]: minimum year 2 HIV-seroprevalence rates detectable with power $1-\beta = 0.90$, one-tailed $\alpha = 0.05$; by sample size and year 1 seroprevalence rates[2]

	Year 1 seroprevalence rate (percent)			
Sample size	0.01	0.10	1.0	2.0
8,000	0.094	0.248	1.367	2.498
16,000	0.059	0.195	1.250	2.344
50,000	0.029	0.147	0.136	2.188
75,000	0.025	0.138	1.100	2.153
100,000	0.023	0.133	1.095	2.133
300,000	0.017	0.118	1.054	2.043

[1]See reference *26*.
[2]For example, if the initial seroprevalence is 0.01 percent, a sample size of 5,000 can show a change that is statistically significant ($\alpha = 0.05$) only if the year 2 observed seroprevalence is at least 0.2 percent.

Processing specimens for HIV testing. Hospitals send completed specimen collection cards to the State or regional neonatal screening laboratory. There the specimens are tested for metabolic and other disorders, as required by the State. After completion of metabolic screening procedures, (*a*) personal identifiers (for example, patient's, name, identification number, accession number) are removed; (*b*) the specimen and corresponding demographic and geographic data are assigned a random survey number; (*c*) the data are entered directly into a computer file or recorded on a CDC

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seroprevalence survey data collection form; and (*d*) specimens labeled with the survey number are sent to the HIV testing laboratory. In two States the specimens are processed and batched according to month and year of birth and in two States, according to month and year of birth and hospital location; no demographic information is retained.

Sample size considerations. For the first survey periods, minimum sample sizes for estimating statewide seroprevalence with bounds of 50 percent relative error were calculated by using seroprevalence rates observed in civilian female applicants for military service. During the survey period, dried blood spots from all births having an adequate specimen (excluding duplicates which may be repeat specimens from the same newborn or specimens from multiple births) are tested for HIV antibodies. The length of the initial survey period is determined by the number of months needed to achieve the minimum sample size. Prevalence rates observed in the first survey period can then be used to calculate minimum sample sizes for subsequent survey periods.

To monitor trends of infection over time, surveys of periods less than 12 months will be repeated annually, during the same months. Detecting changes in seroprevalence over time in a population with a relatively low prevalence requires larger sample sizes. Table 4 shows the change in seroprevalence from year 1 to year 2 that could be detected with 90 percent power ($1-\beta$) and a level of significance of 5 percent for given sample sizes. In States with few births or in smaller geographic areas of States with many births, the number of women giving birth in the area may be insufficient to provide (*a*) estimates of prevalence with the desired precision or (*b*) adequate power to detect changes in prevalence over time. However, the testing of all dried blood spots with adequate specimen during a survey period minimizes sampling error, which improves the precision of the estimates for the survey period. In some States where minimum sample size could be achieved in 3 months and additional resources were available, sample sizes and corresponding survey periods were extended to increase the precision of the estimates.

Demographic and geographic information collected with specimens. The demographic and residential information on mother and infant that is routinely recorded on metabolic screening specimen collection cards varies from State to State. The number of States recording various items for each specimen follows:

Item	*Number of States*
Month of birth	38
Quarter of birth	5
Mother's residence	33
Hospital location	34
Zip code of mother's residence[1]	28
Mother's racial or ethnic group[1]	28
Mother's age group[1]	24

[1] When available from specimen collection card and individual persons cannot be identified through inadvertent disclosure.

In practice, some specimen collection cards are not fully completed by hospital staff before being submitted to the neonatal screening laboratory. In most participating States, plans have been developed to obtain missing information by communicating with the hospitals before specimens are processed for HIV testing to ensure complete recording of data on specimen collection cards. (Copies of the data form used in the newborn seroprevalence survey can be obtained from the authors.)

Assurance of anonymity: aggregation of variable categories. To protect against inadvertent linkage of test results to identifiable individuals, the person(s) processing specimens and recording demographic information cannot also test the specimens or have access to individual test results. Before the first survey period, States must determine which demographic and geographic variables will be retained. The combination of demographic information retained with the specimens must not identify a mother or an infant. Demographic and geographic categories may be aggregated so that the number of women giving birth for each combination of month and year, geographic location, age group, and racial and ethnic group categories is equal to or greater than 3 (*16*). To keep as much useful demographic detail as possible, the following sequence is specified for aggregation of data:

1. Aggregate sparsely populated counties or counties with only one hospital into geographic areas of two or more counties;

2. Recode month of birth to quarter year;

3. Delete county of hospital location if information on county of mother's residence is available;

4. Use 10– or 20–year age group categories; and

5. Aggregate racial and ethnic group categories into broader groups.

Specimen collection and serologic tests. Whole blood is collected from infants via heel-stick puncture and adsorbed onto Schleicher and Schuell Grade 903 Specimen Collection Paper for neonatal screening (*17*). Testing is usually performed within 45 days of collection; dried specimens that cannot be tested within 30 days of collection are stored at 4° C in airtight plastic bags containing dessicant packages and humidity indicator cards (*18*).

Tests for HIV antibody are performed after completion of neonatal screening and after personal identifiers have been removed. A ¼ inch (6.3 mm) circle is punched from the remaining specimen, eluted, and tested for maternal HIV antibodies by using an enzyme immune assay (EIA). Repeatedly reactive specimens are confirmed by Western blot. An EIA kit that is licensed by the FDA for use with plasma or serum and that has shown suitability for use with dried blood spots for blinded HIV seroprevalence surveys (one of five kits, as of September 1989: Abbott, Dupont, Electro-Nucleonics, Genetic Systems, and Organon Teknika Vironostica) is used according to methods and procedures recommended by CDC and NICHD (*18*). Repeatedly reactive specimens are confirmed by Western blot using the Miniblotter system. To ensure consistency, the protocol recommends that the same EIA test kit be used for an entire survey period. All laboratories involved in the survey participate in the CDC Program of Quality Assurance for HIV Seropositivity of Dried Blood Spots (*19*).

Linkage of demographic data and test results. Test results and demographic information with the corresponding survey number are entered separately into a computerized database at the State health department. Data files from each State participating in the survey are shared with CDC and merged into a national master file.

Uses of Seroprevalence Data

These surveys will provide relatively unbiased estimates of HIV prevalence in the population of women giving birth to children during the survey period. These estimates will help health departments to develop and use effectively routine testing, counselors, educational materials, and prevention messages. They can also be used to evaluate the impact of these activities on transmission of HIV. Estimates of prevalence by local geographic area and demographic subgroup will help to identify areas and groups experiencing the greatest impact from HIV and help to establish priorities for prevention and services. Areas with higher seroprevalence rates will need additional resources for HIV testing, post-test counseling, and health care. Areas and groups with lower estimates of seroprevalence will benefit from appropriate counseling programs and age group-specific and culturally appropriate education and prevention messages.

Seroprevalence data from repeated annual surveys will serve to monitor trends of infection over time. This information can be used to obtain estimates of incidence (*20, 21*) and to develop and validate mathematical models that will assist in understanding the dynamics of the HIV-AIDS epidemic.

An important use of the data provided by this survey will be to project the numbers of women and perinatally infected children who will develop AIDS. Recently, the incidence of pediatric AIDS in the United States was calculated indirectly by applying results from perinatal transmission studies (*22*). Projections of pediatric AIDS cases can be used to assess the completeness of reporting in case surveillance and to plan for health care and social services.

Interpretation of Data

The estimates provided by this survey refer directly to the population of women giving birth to live children, not to newborns or to all women of reproductive age. The accuracy with which prevalence rates observed in childbearing women estimate HIV prevalence in women of reproductive age will need to be carefully evaluated. Compared with all women of reproductive age, women delivering live children, on the average, are from households with lower incomes and include a greater proportion of women from minority groups and residents of central metropolitan areas. Thus, unadjusted, crude seroprevalence rates observed in the surveys could overestimate the rate in women of reproductive age. On the other hand, seroprevalence in women of reproductive age could be underestimated by the survey. Prevalence of HIV in women of reproductive age increases with age (reference *11* and "Active Surveillance for Human Immunodeficiency Virus in the U.S.: Early Findings from Sentinel Hospitals," unpublished manuscript by Michael E. St. Louis et al.), and the subgroup of women delivering live children are,

on the average, younger than women of reproductive age. Moreover, the crude prevalence observed from the survey could be underestimated if HIV infection adversely affects pregnancy outcome or if HIV-positive women selectively avoid pregnancy or terminate their pregnancy.

Legal and Ethical Considerations

Before the surveys were begun, the protocol for the Survey of Childbearing Women was reviewed and approved by the Human Subjects Review Committee at CDC and by local institutional review boards and legal authorities in participating States.

These surveys should not replace HIV counseling and testing programs in family planning, prenatal health care, or hospital delivery settings but should be conducted concurrently with these programs. CDC recommends that women of childbearing age at increased risk of infection or in high prevalence populations, regardless of the health care setting, be routinely counseled and encouraged to be tested for HIV antibodies (*23*). Women with HIV infection should be clinically and immunologically evaluated every 6 months, or more frequently, to evaluate the potential benefit of therapy such as prophylactic therapy to prevent *Pneumocystis carinii* pneumonia (*24*). In high prevalence geographic areas or communities, pregnant women should routinely be counseled and encouraged to be tested for HIV antibody as early as possible.

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