II. Newborn Seroprevalence Study: Methods and Results

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Introduction

The New York State Department of Health's ongoing study of HIV infection in childbearing women is based on testing of blood specimens obtained from all infants born in this state for seven inherited metabolic disorders. The specimens are collected and initially tested by the Department's Newborn Screening Program. The specimens are then sent to the HIV Seroprevalence Laboratory for blind HIV testing. This paper describes the results for specimens collected during the 28-month period from November 30, 1987 through March 31, 1990.

Since maternal IgG antibodies cross the placenta, the presence of antibodies in a newborn is indicative of infection in the mother. These antibodies do not necessarily indicate that the child is infected. However, an estimated 30–50 percent of seropositive newborns are actually infected.[1–3]

Methods

Testing Protocol

The protocol for HIV testing of newborn blood specimens has been described in detail by Novick, *et al.*[4] Briefly, a dried-blood specimen is obtained from each infant along with certain demographic information, including the mother's age, zip code and county of residence, the newborn's race/ethnicity, and the month and year of birth. Hospitals are informed of the need for accurate, complete reporting and are contacted, if necessary, to obtain missing information. For the HIV study the demographic information—but not identifying information—is entered into a separate, unlinked data base, where each record is identified by a unique, randomly generated number. The same number is assigned to a portion of the blood specimen. All metabolic disorder screening tests are completed before specimens are submitted for HIV testing.

Specimens for which insufficient or unsuitable blood is left after the metabolic disorder screening are excluded from the blinded HIV seroprevalence study. The number of these specimens is carefully tracked. Repeat specimens cannot be obtained at this stage because the blinding process makes it impossible to link the identity of the infant to the specimen. To ensure that only one specimen representing each childbearing woman is tested, the following are also excluded: all specimens except one from a multiple birth event and all repeat specimens requested for follow-up by the Newborn Screening Program (Figure 1).

Repeat Live Births during Study Period

The likelihood that some women would present with a live birth on more than one occasion during the study period was estimated using Vital Records birth files for 1988 and 1989. Although the Vital Records and HIV newborn data are not directly comparable, this method provides a rough estimate of the percentage of women in the HIV newborn study who had two or more separate live birth deliveries during the study period.

Overall, 3.7 percent of the live-birth records indicated a previous live birth within the same two-year period, 1988–89. However, 29 percent of the New York City records and 11 percent of the remaining records were excluded from this analysis because of incomplete or inaccurate information on the date of the last live birth.

Definition of Test Results

Since the initiation of the Newborn Seroprevalence Study, three sets of crite-

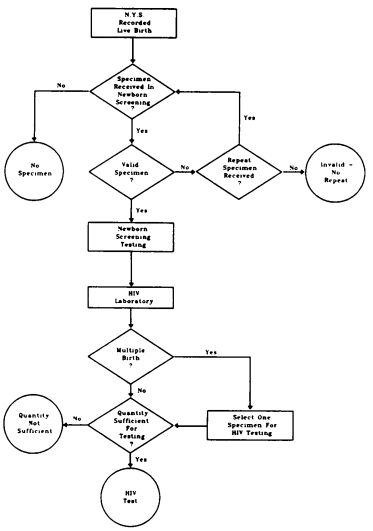

FIGURE 1—New York State Newborn Screening/Newborn HIV Seroprevalence Testing Process

ria have been used to interpret the Western blot results. Reactives were defined as follows:

- Criteria I (November 30, 1987–March 31, 1988): All three of the following: Envelope (gp 41 or gp 120/gp 160), core (p24), and polymerase (p31, p51, or p66).
- Criteria II (April 1, 1988–June 26, 1989): Envelope and either core or polymerase, as defined above.
- Criteria III (June 27, 1989 to present): Any two of the following: p24, gp41, and (gp120 and/or gp160).[5]

Equivocals were defined as virus-specific bands other than the set described above. Nonreactives displayed no virus-specific bands.

Since the individual Western blot band results are currently not available prior to August 1988, the effect of the change from Criteria I to Criteria II could not be examined. However, the change from Criteria II to Criteria III was examined by applying Criteria II to the specimens tested June 27, 1989 to present and comparing the number and percent HIV positive to that found under Criteria III. Under Criteria II there were 1,918 HIV positives with a seroprevalence rate of 0.661 percent. This was nearly identical to that found under Criteria III with 1,921 HIV positives and a seroprevalence rate of 0.662 percent.

Statistical Analysis

Seroprevalence rates were calculated based on the number of Western blot reactives and total specimens tested, excluding equivocals. We could not obtain a second sample for reevaluation of equivocals because of the blinded nature of the study.

Age/race-specific HIV seroprevalence rates were calculated for five racial/ethnic subgroups (White, Black, Hispanic, Other, and Unknown), and six maternal age categories (<20 years, 20–24 years, 25–29 years, 30–34 years, 35+ years and Unknown).

Geographic rates were calculated for New York City total, each of the five New York City boroughs, New York State exclusive of New York City, and four regions outside New York City, which were selected on the basis of urbanization, physical proximity to New York City, and cumulative incidence of AIDS to date. The four regions were New York City Suburban (Nassau, Suffolk, Westchester, and Rockland counties), Mid-Hudson Valley (Dutchess, Putnam, Orange, Sullivan, and Ulster counties), Upstate Urban (Albany, Schenectady, Onondaga, Monroe, and Erie counties), and Upstate Rural (all other counties in the state).

For New York City the HIV seroprevalence rates were also calculated for each zip code area and mapped by quartiles. Zip code areas with fewer than 100 births were eliminated from this mapping. For New York State exclusive of New York City, due to the large number of zip code areas and the small number of births within each area, only the rates for areas with two or more HIV-positive cases and rates twice that of the overall rate were examined, and the rates were mapped by county.

Trend analysis was conducted on the monthly HIV seroprevalence rates for births occurring in the 27-month period, December 1987 through February 1990. Births occurring in November 1987 were excluded from this analysis because the specimens received beginning November 30 covered two-thirds of the November newborns. Plots of the monthly rates were analyzed by simple regression techniques[6–8] with SAS software.[9] A coefficient of determination (R^2) was calculated to determine the proportion of the variation in rates explained by the independent variable, time (month of birth). The 95 percent confidence intervals for the predicted value were also calculated.

This procedure was performed for all of New York State, all of New York City, all of New York State exclusive of New York City, each of the five New York City boroughs, and each of the four other regions described above. The data for all of New York State, all of New York City, and all of New York State exclusive of New York City were further analyzed for three maternal age groups (<20, 20–29, 30+) and for three race/ethnicity groups (White, Black, and Hispanic).

Results

During the study period November 30, 1987 through March 31, 1990, a total of 653,328 blood specimens were analyzed for HIV serologic status, of which 211 equivocals (0.03 percent) were eliminated from the analysis. Of the remaining 653,117 specimens, 10,125 were from women residing outside of New York State, and 2,408 were from women whose residence was unknown. These specimens were also eliminated from the analysis. For the remaining 640,584 specimens, the overall seroprevalence rate was 0.66 percent: 1.24 percent in New York City and 0.17 percent in the rest of the State.

New York City

The HIV seroprevalence rates for New York City and each borough are shown in Table I-1. The rates were highest in the Bronx, followed by Manhattan and then Brooklyn. The rates for Queens and Staten Island were more than twice the rates for the two New York State regions adjacent to New York City, New York City Suburban, and Mid-Hudson Valley.

Of the 170 zip code areas in New York City with 100 or more births, 31 (18.2 percent) had HIV seroprevalence rates in excess of 2 percent and 13 (7.6 percent) had rates in excess of 3 percent. The distribution by quartiles is shown in Figure 2.

The vast majority of HIV seropositives in New York City (89.3 percent) were Black or Hispanic, although only 60.8 percent of newborns were Black or Hispanic.

The highest rates were detected among Black and Hispanic newborns. These rates increased with maternal age for Blacks and Hispanics but not for Whites or Other (Table II-2). The rates for both Black and Hispanic infants peaked in the 30–34 year maternal age group.

Age-specific seroprevalence rates are plotted in Figure 3. The sharpest rise is seen in New York City for infants born to mothers between ages 14 and 24. These rates increased ninefold, from 0.16 percent (1 in 624) for 14-year-olds to 1.41 percent (1 in 71) for 24-year-olds.

TABLE II-1—Percent of HIV Positive Newborns by Region for New York State, November 30, 1987–March 31, 1990

Region	Number Positive	Total Tested	Percent Positive
New York State Exclusive of New York City	601	346,522	0.17
NYC Suburban	329	120,422	0.27
Mid-Hudson Valley	71	29,450	0.24
Upstate Urban	119	88,088	0.14
Upstate Rural	82	108,562	0.08
New York City	3,650	294,062	1.24
Manhattan	799	50,364	1.59
Bronx	998	58,003	1.72
Brooklyn	1,352	104,613	1.29
Queens	424	67,474	0.63
Staten Island	77	13,608	0.57

Women with White seropositive infants were slightly younger (mean 28.6 years) than women with White seronegative infants (29.2 years). Women with Black seropositive infants were significantly older than women with Black seronegative infants (28.2 versus 26.0 years). Women with Hispanic seropositive infants were also significantly older (27.2 versus 25.7 years).

New York State Exclusive of New York City

Seroprevalence rates for New York State and its four regions exclusive of New York City are shown in Table II-1. Rates for two regions adjacent to New York City (New York City Suburban and Mid-Hudson Valley) were only about one-fifth the rate for New York City but twice or three times the rates for the other regions.

HIV seroprevalence was concentrated in certain areas of the state (Figure 4). In New York State exclusive of New York City, 64 zip code areas had two or more seropositives and a HIV seroprevalence rate more than double the average for all areas outside New York City. Of the 64 zip code areas, 50 had rates of 0.5 percent or higher. The 64 zip code areas contained 65 percent of the HIV seropositives but only 16 percent of the newborns tested outside of New York City.

In New York State exclusive of New York City, HIV seroprevalence was highest for Black newborns followed by Hispanics (Table II-3). The majority of HIV seropositives (69.4 percent) were either Black or Hispanic, although only 14.0 percent of the newborns tested were Black or Hispanic. For Black newborns the HIV seroprevalence rate increased with maternal age, peaking in the 35+ age group. For Hispanic newborns the rate increased only in this maternal age group. For White newborns no significant variation with maternal age was found.

As seen in New York City, mothers of White seropositive infants were on average slightly younger than those with White seronegative infants (26.5 years vs 27.7 years); however, the difference is significant in women in New York State exclusive of New York City. Women with Black seropositive infants were significantly older than those with Black seronegative infants (27.7 years vs 24.6 years). Mothers of Hispanic newborns were 1.1 years older (26.5 years vs 25.4 years).

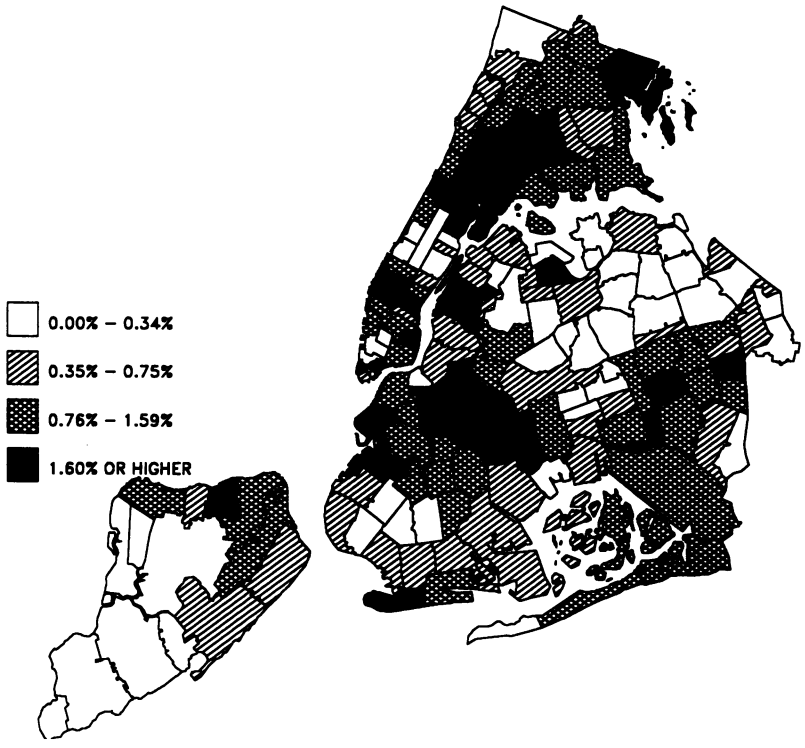

FIGURE 2—HIV Seroprevalence in New York City by Zip Code, November 30, 1987–March 31, 1990

Trend Analysis

When HIV seroprevalence rates were plotted by month of birth for New York City and for New York State exclusive of New York City, with 95 percent confidence intervals, neither slope was significantly different from zero. No significant increase or decrease was found for any borough of New York City, any region outside of New York City, or any three racial/ethnic subgroups in New York State exclusive of New York City.

Only two age groups showed evidence of a statistically significant trend for the 27-month period. For New York City women less than 20 years old (Figure 5A), the rate declined slightly ($y = 0.00785 - 0.000132 \times$, $p < .01$). The standard error of the slope was 0.0000486. However, the coefficient of determination (R^2) was only .23, explaining only a small proportion of the variation in the rate.

TABLE II-2—Distribution of HIV Positive Newborns by Maternal Age and Race/Ethnicity for New York City, November 30, 1987–March 31, 1990

Race/Ethnicity	HIV Positive by Maternal Age Group (years) <20	20–24	25–29	30–34	35+	Unknown	Total
White							
HIV Positive							
Percent	0.22	0.42	0.38	0.29	0.28	0.74	0.34
Number	6	58	102	74	41	3	284
Tested	2,716	13,935	27,158	25,715	14,403	408	84,335
Black							
HIV Positive							
Percent	0.68	1.68	2.59	3.08	2.98	3.10	2.19
Number	95	429	670	547	268	19	2,028
Tested	14,002	25,512	25,831	17,780	8,985	612	92,722
Hispanic							
HIV Positive							
Percent	0.57	1.26	1.75	1.95	1.42	2.35	1.43
Number	74	333	425	287	101	12	1,232
Tested	12,909	26,519	24,232	14,720	7,113	511	86,004
Other							
HIV Positive							
Percent	0.37	0.43	0.28	0.14	0.23	0.00	0.27
Number	4	23	29	11	8	0	75
Tested	1,095	5,293	10,222	8,037	3,408	147	28,202
Unknown							
HIV Positive							
Percent	0.51	1.10	1.52	0.69	1.76	1.01	1.11
Number	1	5	9	3	4	9	31
Tested	195	454	594	435	227	894	2,799
Total							
HIV Positive							
Percent	0.58	1.18	1.40	1.38	1.24	1.67	1.24
Number	180	848	1,235	922	422	43	3,650
Tested	30,917	71,713	88,037	66,687	34,136	2,572	294,062

For women in New York State exclusive of New York City aged 20–29 (Figure 5B), the rate increased slightly ($y = 0.00149 + 0.00003 \times$, $p < .03$). The standard error of the slope was 0.0000128. R^2 for this group was extremely small (.17).

Discussion

Before this study was implemented, extremely limited information was available on the prevalence of HIV infection in childbearing women. Two recent studies in New York City hospitals revealed an HIV seroprevalence rate of 2.4 to 2.5 percent in infant cord blood specimens.[10,11] A recent Massachusetts Department of Health study found an overall rate of 0.21 percent in anonymously tested newborn blood samples, ranging from 0.1 percent in suburban and rural hospitals to 0.8 percent in inner-city hospitals.[12]

In this study, we found an overall HIV seroprevalence rate of 0.66 percent for childbearing women. The magnitude of this health problem was most striking in New York City where in some zip code areas as many as one out of 22 childbearing women were found to be HIV-infected. For New York State exclusive of New York City the lower overall seroprevalence rate (0.17 percent) is deceptive, because zip code analysis revealed small areas with rates approaching those in New York City. This small-area information is critical for assessment of large geographic areas, where apparently low seroprevalence may mask communities with rates of serious public health concern.

Although 87 percent of the seropositive newborns in New York State were Black or Hispanic, the seroprevalence rate of 0.12 percent for Whites and for other racial/ethnic groups confirms a significant incursion of HIV infection in those populations as well.

The finding of an increased infection rate with increasing maternal age has implications for the design of preventive activities. An especially sharp rise was seen for adolescents and young women in New York City, from 1 in 624 at age 14 to 1 in 71 at age 24 (Figure 3). Preventive efforts must begin with children and younger adolescents to control this rapid spread.

Although racial/ethnic and maternal-age patterns are crucial for projections and resource allocation, the intersection of these patterns offers deeper insight into the environmental factors that determine prevalence. Identifying such cohorts will help to define the relevant exposures, such as patterns of drug use, and thus the targeting of preventive measures. Individuals in younger cohorts with different exposure risks may exhibit substantially different patterns of HIV infection in the future. Those changes will affect not only projections of the epidemic, but also the measures needed to reduce transmission of the virus.

Certain biases inherent in this study may have an impact on the observed rates. Possible bias resulting from newborns not

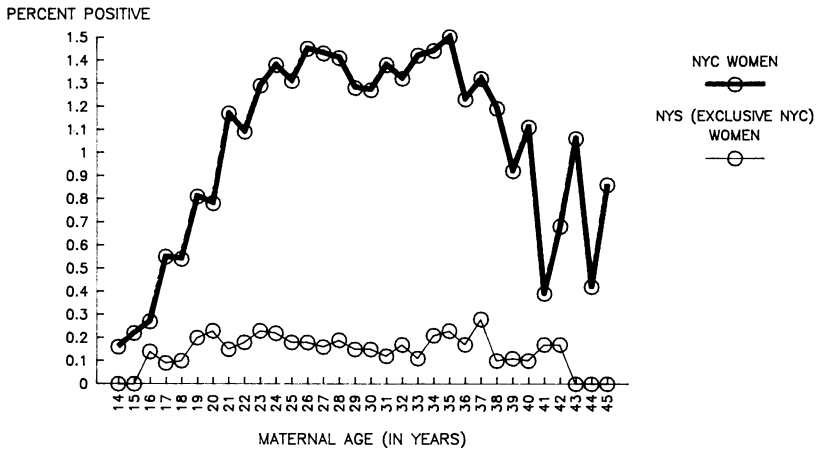

FIGURE 3—HIV Seroprevalence in NYS by Single Year of Maternal Age (November 30, 1987–March 31, 1990)

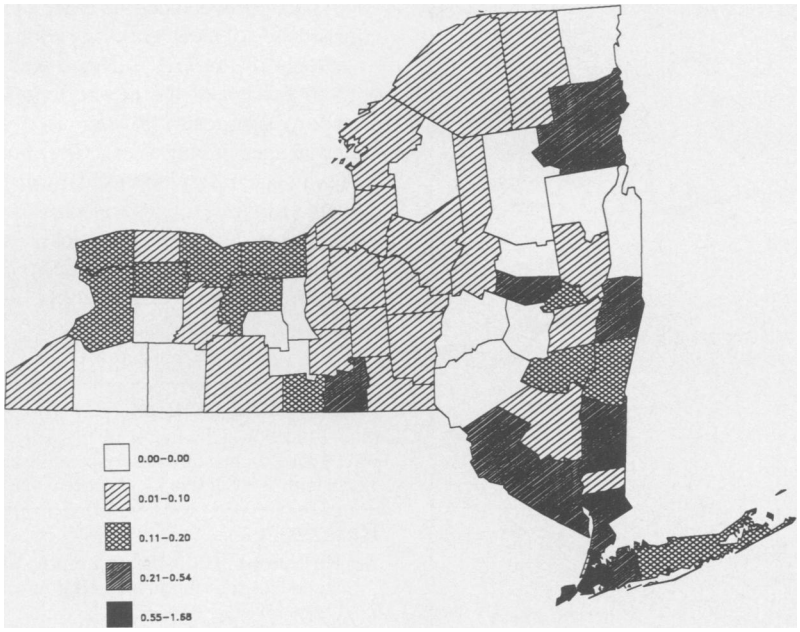

FIGURE 4—HIV Seroprevalence in NYS exclusive of NYC by County (November 30, 1987–March 31, 1990)

TABLE II-3—Distribution of HIV Positive Newborns by Maternal Age and Race/Ethnicity for New York State Exclusive of New York City, November 30, 1987–March 31, 1990

	HIV Positive by Maternal Age Group (years)						
Race/Ethnicity	<20	20–24	25–29	30–34	35+	Unknown	Total
White							
HIV Positive							
Percent	0.05	0.09	0.06	0.04	0.03	0.09	0.06
Number	9	53	57	35	10	1	165
Tested	18,943	59,858	101,038	78,112	29,328	1,095	288,374
Black							
HIV Positive							
Percent	0.26	0.67	1.30	1.60	1.72	1.52	0.95
Number	20	75	120	82	39	2	338
Tested	7,660	11,125	9,245	5,132	2,269	132	35,563
Hispanic							
HIV Positive							
Percent	0.51	0.59	0.55	0.55	1.32	0.00	0.61
Number	10	25	20	11	13	0	79
Tested	1,966	4,243	3,639	1,986	982	51	12,867
Other							
HIV Positive							
Percent	0.00	0.45	0.18	0.13	0.09	0.00	0.19
Number	0	7	5	3	1	0	16
Tested	561	1,563	2,758	2,285	1,058	44	8,269
Unknown							
HIV Positive							
Percent	0.00	0.48	0.00	0.00	0.79	0.20	0.21
Number	0	1	0	0	1	1	3
Tested	56	207	316	246	127	497	1,449
Total							
HIV Positive							
Percent	0.13	0.21	0.17	0.15	0.19	0.22	0.17
Number	39	161	202	131	64	4	601
Tested	29,186	76,996	116,996	87,761	33,764	1,819	346,522

tested is discussed in a later chapter.[13] Another bias could result from double-counting the estimated 3.7 percent of women in the study who may have had two or more separate live birth deliveries within the study period.

Regardless of these biases, data from the seroprevalence study are invaluable in developing estimates of the number of infected women of reproductive age and the number of HIV-infected children. If we assume that 30 percent of seropositive newborns will prove to be infected, 1,275 children with HIV infection were born in New York State during the study period. Yet, only 648 cases of pediatric AIDS had been reported as of March 1990. This gap, attributable mainly to infected but asymptomatic children or those with health problems but no HIV disorder diagnosis, is highly relevant to our understanding of pediatric HIV infection and the need for health care resources.

The few trends found in this study reflect changes in seroprevalence over a brief period of only 27 months. Longer monitoring may be necessary to detect changes in this epidemic. The seroprevalence rates are for a population of childbearing women who have already been infected, plus those infected during the study period, minus those who leave the population by outmigration, death, or aging out of the study. A stable seroprevalence in this limited study may, therefore, be compatible with an actual rising or falling incidence of new infection. The observed trends should also be viewed with caution, because two significant results in 30 separate analyses may be the result of chance alone.

Little information on HIV seroprevalence in newborns is available for the period before late 1987. A rapid increase in HIV infection in childbearing women is assumed to have occurred at some point between 1980 and the present. At the end of 1983, only 174 female AIDS cases had been reported to the New York State AIDS Registry.[14] By the end of March 1990, that number had increased 24-fold to 4,194.[15] The lack of observed trend in the 27-month study period and the increase in infection manifested by AIDS in childbearing women prior to this point suggest a decrease in the rate of increase of the epidemic of HIV infection in childbearing women. However, progress of the epidemic is not likely to be uniform throughout the state with certain lower-prevalence areas possibly exhibiting upward trends in the future.

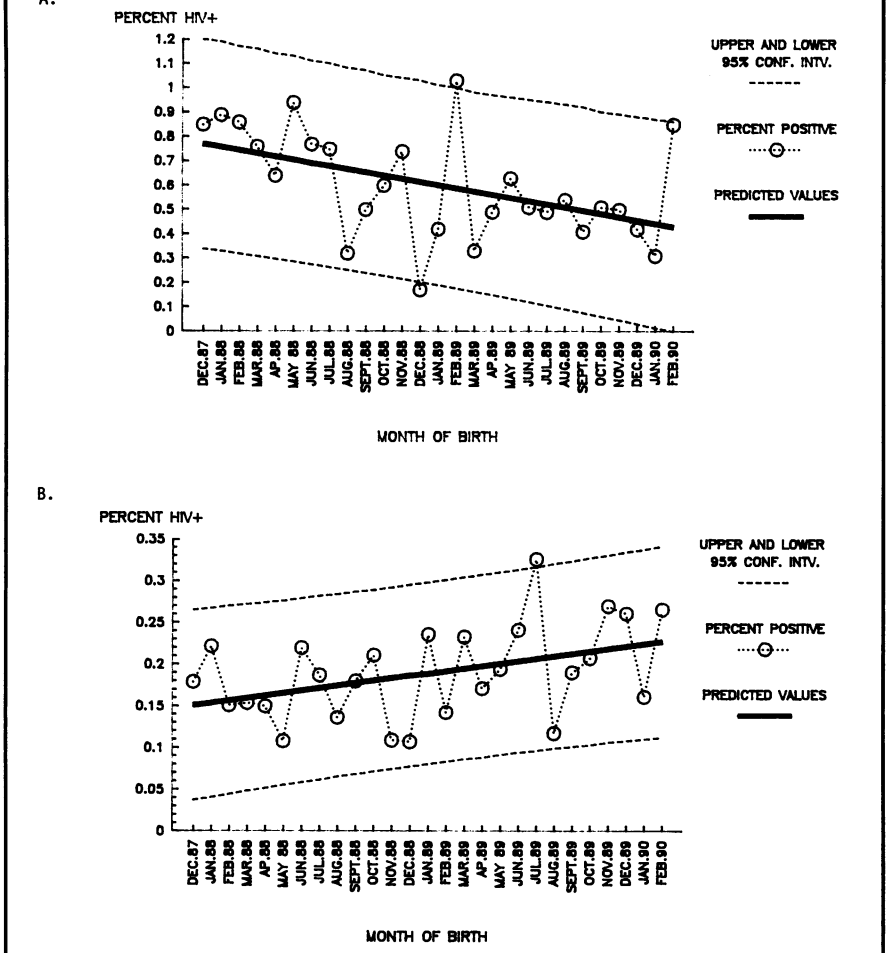

FIGURE 5—Percentage of HIV-Positive Newborns in NYS by Month of Birth for Two Groups with Statistically Significant Trends (December 1987–February 1990)

A—Women less than 20 years old, NYC
B—Women 20–29 years old, NYS exclusive of NYC

Newborn infants of adolescent mothers in New York City showed a decreasing trend in HIV seroprevalence during the 27-month period. This group is particularly critical to the monitoring process as newborns of teenaged mothers have the lowest seroprevalence rates but the greatest rate of increase with maternal age. Seroprevalence among this group may be a closer reflection of recent incidence, since the time interval between HIV infection and childbearing is most likely shorter than that for the older women.

Possible saturation of susceptible individuals in certain geographic areas may also offer an explanation for the lack of observed trends. If so, our efforts toward prevention must be redoubled in these areas, as well as communitywide, to prevent transmission from this pool to others entering various risk groups in the community.

Summary

For the 28-month period, November 30, 1987 through March 31, 1990, 653,117 blood specimens obtained on all newborn infants in New York State for detection of metabolic disorders were also analyzed for HIV serologic status. The overall seroprevalence rate was 0.66 percent: 1.24 percent in New York City and 0.17 percent in New York State exclusive of New York City. Rates of seropositivity were highest in the Bronx (1.72 percent) and Manhattan (1.59 percent). Outside of New York City, HIV seropositivity was concentrated in certain areas. Sixty-four zip codes with two or more seropositives and an HIV seroprevalence rate twice the average outside of New York City contained 65 percent of the HIV seropositives but only 16 percent of the newborns tested. Newborn seropositivity increased with maternal age. In New York City, the seroprevalence rates increased from 0.16 percent (1 in 624) for 14-year-olds to 1.41 percent (1 in 71) for 24-year-olds, a ninefold rise. This survey has provided the impetus for a number of preventive initiatives. □

Acknowledgments

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