The Influence of HIV-1 Exposure and Infection on Levels of Passively Acquired Antibodies to Measles Virus in Zambian Infants

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(See the editorial commentary by Katz on pages 1425–6)

Background. The age at which passively acquired antibodies are lost is critical to determining the optimal age for measles vaccination. Little is known about the influence of human immunodeficiency virus type 1 (HIV-1) infection on levels of prevaccination antibodies to measles virus.

Methods. Antibodies to measles virus were measured by plaque reduction neutralization assay in HIV-1–infected, HIV-seropositive but uninfected, and HIV-seronegative Zambian infants aged 6 weeks to 9 months. Regression models were used to estimate age-specific antibody concentrations.

Results. Neutralizing antibodies to measles virus were measured in 652 plasma samples collected from 448 infants, of whom 61 (13.6%) were HIV-1 infected, 239 (53.4%) were HIV seropositive but uninfected, and 148 (33%) were HIV seronegative. The best fitting model suggests that HIV-1–infected infants have lower levels of passively acquired antibodies to measles virus at birth than do HIV-seronegative infants, but their antibody levels decrease more slowly. By 6 months of age, 91% (95% confidence interval, 83%–99%) of HIV-1–infected infants, 83% (95% confidence interval, 77%–89%) of HIV-seropositive but uninfected infants, and 58% (95% confidence interval, 51%–64%) of HIV-seronegative infants were estimated to have antibody levels that were unlikely to affect immune responses to measles vaccine (cutoff value for immune response, <50 mIU/mL). By 9 months of age, 99% of all infants had antibody levels <50 mIU/mL.

Conclusions. Infants born to HIV-1–infected women are less likely to have passively acquired antibodies that would neutralize measles vaccine virus and, thus, have an increased risk of measles prior to the age of routine vaccination. Protection could be achieved by administration of the first dose of measles vaccine prior to 9 months of age.

Passively acquired maternal antibodies protect young infants against measles but may also impair the immune response to attenuated measles vaccines by neutralizing vaccine virus [1]. Knowledge of the age at which passively acquired antibodies are lost is critical to determining the optimal age of measles vaccination; this age should be chosen to maximize the proportion of infants seroconverting while minimizing the incidence of measles virus at the age of vaccination [2]. In most developing countries, measles vaccine is administered to infants at 9 months of age, when ~85% of infants born to mothers with naturally acquired immunity will respond to vaccination [3]. The age by which passively acquired antibodies to measles virus (MV) are lost depends on maternal antibody levels, the efficiency of placental transfer, and rates of catabolism after birth [4]. The efficiency of placental antibody transfer, an active process that begins at ~28 weeks of gestation, is impaired by maternal malaria and HIV-1 infection [4]. Although several studies have reported that infants born to HIV-1–infected women have lower levels of passively acquired antibodies to MV at birth [5–8], the impact of HIV-1 infection on the rate of decrease of levels of passively acquired neutralizing antibodies to MV during infancy has not been investigated. One study reported a 3.8-fold increase in the risk of acquiring measles before 9 months of age among Kenyan infants born to HIV-seropositive women, compared with those born to HIV-
seronegative women [9]. This increased risk could be because of lower antibody levels at birth and/or more rapid decrease of antibody levels.

Because of the importance for measles vaccination strategies of knowing the age at which passively acquired antibodies to MV are lost, particularly in regions with high HIV-1 prevalence, we compared neutralizing antibody levels to MV in Zambian infants aged 6 weeks to 9 months according to their HIV-1 infection or exposure status.

METHODS

Study population. The study population consisted of infants who participated in an observational study of the immunogenicity of measles vaccine in HIV-1–infected and HIV-1–uninfected Zambian infants [10]. Infants attending a public clinic for routine diphtheria-pertussis-tetanus and polio vaccinations from May 2000 through November 2002 who had not been vaccinated against measles and who resided in Chawama Township, Lusaka, Zambia, were invited to participate. Caregivers from whom written informed consent was obtained were interviewed using a standard questionnaire to obtain the infant’s vaccination history, details of illness at the time of the interview, and history of a measles-like illness. Blood samples were obtained by venipuncture, placed in EDTA tubes, and transported to the Virology Laboratory (University Teaching Hospital, Lusaka, Zambia) for screening for antibodies to HIV. All HIV-seropositive infants were enrolled; a random sample of HIV-seronegative infants was also enrolled. Infants were vaccinated with standard-titre Edmonston-Zagreb measles vaccine (Berna Biotec, formerly Swiss Serum and Vaccine Institute) at ∼9 months of age, at which time a second questionnaire was administered to obtain information on the infant’s health and a second venous blood sample was obtained.

Laboratory assays. Blood samples were tested for antibodies to HIV by rapid immunoassay (Determine HIV-1/2, Abbott Laboratories). HIV-1 infection was determined in each HIV-seropositive infant by detection of HIV-1 RNA using RT-PCR (Amplicor HIV-1 Monitor, version 1.5, Roche Molecular Systems). A modified plaque reduction neutralization assay was used to measure antibodies to MV, as described elsewhere [11]. Plasma samples were tested in parallel with the Second International World Health Organization Serum Standard (66/202), with a titer of 1:8 corresponding to 8 mIU/mL.

Statistical analysis. Data were entered twice, checked, and validated using Epilinfo, version 6.04 (Centers for Disease Control and Prevention). Stata, version 9 (Stata), was used for analysis. We classified the HIV infection or exposure status of infants as (1) HIV-1–infected if HIV-1 RNA was detected in any plasma sample obtained before or at the time of vaccination, (2) HIV-seropositive but uninfected if antibodies to HIV were detected and no HIV-1 RNA was detected, and (3) HIV-seronegative if no antibodies to HIV were detected. Infants with confirmed wild-type MV infection (defined as clinical measles [12], with the presence of MV-specific IgM antibodies) or probable wild-type MV infection (defined as a 4-fold increase in MV-specific IgG antibody level before vaccination) were excluded from analyses.

Weight-for-height, weight-for-age, and length-for-age z scores were calculated with growth reference curves developed by the National Center for Health Statistics and Centers for Disease Control and Prevention [13]. Z scores of ≤−2 were considered to represent poor anthropometric status. Infants with a poor length-for-age z score were considered to be stunted, infants with a poor weight-for-age z score were considered to be underweight, and infants with a poor weight-for-length z score were considered to be wasting. Geometric mean antibody concentrations and their 95% CIs were estimated, assigning a value of 2 mIU/mL to samples with titers <1:8.

Linear regression was used to model the association between HIV-1 exposure or infection and log antibody concentrations to MV, to estimate antibody levels to MV at birth, and to estimate the rate of antibody level decrease by HIV-1 exposure and infection status. To account for the fact that some infants contributed 2 samples (at screening and at the time of vaccination), random effects models were used to model within-infant correlation. Antibody levels of 50–120 mIU/mL were considered to be sufficient to interfere with immune responses to measles vaccine but insufficient to protect against wild-type MV infection [14]. Antibody levels ≤50 mIU/mL were considered to be nonprotective and insufficient to interfere with immune responses to measles vaccine [15, 16]. Antibody levels ≥120 mIU/mL were considered to be protective, although data on protective levels of passively acquired antibodies to MV are not available. The levels of passively acquired antibodies that are necessary for protection may be higher than those needed after vaccination or infection, because cell-mediated immunity is lacking. The proportion of infants with antibody levels above these thresholds during the first 9 months of life was estimated, assuming that log concentrations are normally distributed with a standard deviation estimated from the random effects models. Ninety-five percent CIs were obtained using the bootstrap method [17]. The half-life of passively acquired MV antibodies (i.e., the length of time required for the antibody concentration to become one-half of the original concentration) was determined for each HIV-1 exposure and infection group.

Four models were examined on the basis of different assumptions regarding the variability between HIV-1 exposure and infection groups: model 1 assumed that the mean anti-MV antibody level at birth and the rate of decrease of passively acquired anti-MV antibody levels were the same for all infants, model 2 assumed that the mean anti-MV antibody level at birth was the same for all infants but the rate of decrease of passively
acquired anti-MV antibody levels varied by HIV-1 exposure or infection status, model 3 assumed that the mean anti-MV antibody level at birth varied by HIV-1 exposure or infection status but the rate of decrease of passively acquired anti-MV antibody levels was the same in all groups, and model 4 assumed that both the mean anti-MV antibody level at birth and the rate of decrease of passively acquired anti-MV antibody levels varied by HIV-1 exposure or infection status. The likelihood ratio test was used to compare the different models.

We also investigated maternal age, sex, wasting, stunting, underweight, and illness at the time of sampling as potential predictors of anti-MV antibody levels. For multivariable analyses, variables were retained in the model if they were not considered to be on the causal pathway between HIV-1 infection and passively acquired antibody levels, were statistically associated with antibody levels ($P < .05$), or substantially altered estimates of the association of the primary exposure variable (HIV-1 infection or exposure status). Illness at the time of sampling and malnutrition were considered to be on the causal pathway between HIV-1 infection and passively acquired antibody levels and, therefore, were excluded from the multivariable analysis.

**RESULTS**

Neutralizing antibodies to MV were measured in 719 plasma samples obtained from May 2000 through November 2002 from 497 infants prior to measles vaccination. Excluded from the analysis were samples collected from 34 HIV-seropositive infants in whom HIV-1 infection status was not determined and 14 infants with confirmed or probable measles. An additional 14 infants were suspected to have had measles between screening and vaccination, and samples obtained from these infants at the time of vaccination were excluded from the analysis. Samples obtained at the time of measles vaccination from 2 infants who were aged $\geq 20$ months were also excluded (1 of these infants contributed a screening sample). Thus, the analysis included measures of neutralizing antibodies from 652 plasma samples collected from 448 infants, of whom 13.6% were HIV-1 infected, 53.4% were HIV seropositive but uninfected, and 33% were HIV seronegative. Antibodies to MV were measured at both prevaccination and vaccination visits in 204 infants (mean duration from the prevaccination visit to the vaccination visit $\pm SD, 5.2 \pm 1.3$ months), at only the prevaccination visit in 83 infants, and at only the vaccination visit in 161 infants.

Mothers of HIV-1–infected infants tended to be older (median age, 28 years; IQR, 25–31.5 years) than mothers of HIV-seropositive but uninfected infants (median age, 25 years; IQR, 22–29 years) and mothers of HIV-seronegative infants (median age, 24 years; IQR, 21–27 years). There were no major differences in sex, median age at screening, or median age at measles vaccination among infants according to HIV-1 exposure or infection status (table 1). HIV-1–infected infants were more likely to be underweight (28% of HIV-1–infected infants; $P < .001$), stunted (50%; $P = .04$), or experience wasting (6%; $P = .01$) than were HIV-seropositive but uninfected infants (10%, 35%, and 1.4% of HIV-seropositive but uninfected infants, respectively) and HIV-seronegative infants (8.5%, 37%, and 1% of HIV-seronegative infants, respectively). HIV-1–infected infants were also more likely to be ill at the time of sampling (41%) than were HIV-seropositive but uninfected infants (30%) and HIV-seronegative infants (25%; $P = .03$).

Among infants aged <7 months, neutralizing antibody levels to MV were highest in HIV-seronegative infants and lowest in HIV-1–infected infants (figure 1). The model allowing the rate of antibody level decrease to vary by HIV-1 exposure or infection status provided a better fit than the model assuming a similar rate of antibody level decrease (model 2 vs. model 1; $P = .03$), and the model allowing antibody levels at birth to vary provided a better fit than the model assuming a similar antibody level at birth (model 3 vs. model 1; $P < .001$). The best fitting model was achieved by allowing both antibody levels at birth and the rate of antibody level decrease to vary by HIV-1 exposure or infection status (model 4; table 2). The results of this model suggest that infants born to HIV-1–infected mothers have lower levels of passively acquired antibodies to MV at birth than do HIV-seronegative infants, but their antibody levels decrease more slowly. HIV-1–infected infants were estimated to have antibody levels at birth that were one-seventh of those in infants born to HIV-uninfected mothers. Being underweight or ill at the time of sampling was associated with low antibody levels in univariable analysis but not after adjustment for the infant’s age. Associations between HIV-1 exposure status and antibody levels to MV were not adjusted for being underweight or ill, because these factors were considered to be influenced by HIV-1 infection. No other factors were associated with antibody levels.

Figure 2 shows the proportion of infants with detectable antibodies to MV and infants with antibody levels $\geq 50$ mIU/mL and $\geq 120$ mIU/mL, by age in weeks, according to HIV-1 exposure or infection status, and estimated using model 4. At birth, a higher proportion of HIV-seronegative infants were estimated to have antibody levels $\geq 120$ mIU/mL (99.9%; 95% CI, 97.2–100), compared with HIV-seropositive but uninfected infants (96%; 95% CI, 89.9–100) and HIV-1–infected infants (65%; 95% CI, 40.9–89.9). By 6 months of age, 91.1% (95% CI, 83.2–99.0) of HIV-1–infected infants, 83.3% (95% CI, 77.9–88.6) of HIV-seropositive but uninfected infants, and 57.7% (95% CI, 51.2–64.2) of HIV-seronegative infants were estimated to have antibody levels to MV $< 50$ mIU/mL. By 9 months of age, 99% of all infants had antibody levels $< 50$ mIU/mL, regardless of HIV-1 exposure or infection status.

The half-life of neutralizing antibodies to MV was estimated
Table 1. General characteristics of infants, by HIV infection or exposure status of the child.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>HIV seronegative</th>
<th>HIV seropositive but uninfected</th>
<th>HIV-1 infected</th>
<th>P&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal age</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>&lt;19 years</td>
<td>14 (10)</td>
<td>11 (5)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>20–24 years</td>
<td>46 (31)</td>
<td>97 (41)</td>
<td>14 (23)</td>
<td></td>
</tr>
<tr>
<td>25–29 years</td>
<td>36 (24)</td>
<td>71 (30)</td>
<td>24 (39)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>&gt;29 years</td>
<td>18 (12)</td>
<td>53 (22)</td>
<td>22 (30)</td>
<td></td>
</tr>
<tr>
<td>Missing data</td>
<td>34 (23)</td>
<td>7 (3)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>71 (48)</td>
<td>124 (52)</td>
<td>25 (42)</td>
<td>.3</td>
</tr>
<tr>
<td>Female</td>
<td>77 (52)</td>
<td>115 (48)</td>
<td>36 (59)</td>
<td></td>
</tr>
<tr>
<td>Age at time of screening, median months (IQR)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>4.1 (3.3–5.3)</td>
<td>3.8 (3.2–4.6)</td>
<td>4.0 (3.2–5.1)</td>
<td>.3</td>
</tr>
<tr>
<td>Age at time of vaccination, median months (IQR)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>9.1 (9.0–9.3)</td>
<td>9.1 (9.0–9.3)</td>
<td>9.0 (9.0–9.2)</td>
<td>.6</td>
</tr>
</tbody>
</table>

NOTE. Data are no. (%) of infants, unless otherwise indicated. IQR, interquartile range.

<sup>a</sup> Age and sex comparisons were determined by χ<sup>2</sup> test, and age at screening and age at vaccination comparisons were determined by Kruskal-Wallis test.

<sup>b</sup> Data are for 97 HIV-seronegative infants, 153 HIV-seropositive but uninfected infants, and 37 HIV-1–infected infants.

<sup>c</sup> Data are for 103 HIV-seronegative infants, 213 HIV-seropositive but uninfected infants, and 49 HIV-1–infected infants.

To be 6.3 weeks (95% CI, 5.8–6.8). The estimated half-life was shortest for HIV-seronegative infants (5.6 weeks; 95% CI, 5.0–6.4), intermediate for HIV-seropositive but uninfected infants (6.4 weeks, 95% CI, 4.8–9.3), and longest for HIV-1–infected infants (8.5 weeks; 95% CI, 5.5–18.6).

DISCUSSION

Levels of passively acquired neutralizing antibodies to MV were lower during the first 9 months of life in Zambian infants born to HIV-1–infected women than in infants born to uninfected women; in addition, these levels were lower in HIV-1–infected infants than in HIV-seropositive but uninfected infants. As a consequence, infants born to HIV-1–infected women and particularly HIV-1–infected infants are at increased risk of measles prior to the age of routine vaccination but are also less likely to have levels of passively acquired antibodies that would neutralize measles vaccine virus.

Our model suggests that levels of passively acquired neu-
Table 2. Predicted measles antibody levels at birth and decrease in antibody levels, by HIV-1 infection or exposure status of the infant.

<table>
<thead>
<tr>
<th>Model</th>
<th>Predicted GMC at birth (95% CI)</th>
<th>Predicted difference in antibody levels at birth, % (95% CI)</th>
<th>Predicted half-life, weeks (95% CI)</th>
<th>P^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV seronegative</td>
<td>517 (388–689)</td>
<td>...</td>
<td>6.3 (5.8–6.8)</td>
<td></td>
</tr>
<tr>
<td>HIV seropositive</td>
<td>517 (388–689)</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>HIV-1 infected</td>
<td>517 (388–689)</td>
<td>...</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Model 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV seronegative</td>
<td>506 (380–674)</td>
<td>...</td>
<td>6.8 (6.1–7.5)</td>
<td></td>
</tr>
<tr>
<td>HIV seropositive</td>
<td>506 (380–674)</td>
<td>...</td>
<td>6.1 (5.3–7.3)</td>
<td>.03^b</td>
</tr>
<tr>
<td>HIV-1 infected</td>
<td>506 (380–674)</td>
<td>...</td>
<td>6.1 (5.1–7.6)</td>
<td></td>
</tr>
<tr>
<td>Model 3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV seronegative</td>
<td>717 (516–996)</td>
<td>Baseline</td>
<td>6.3 (5.9–6.8)</td>
<td>&lt;.001^c</td>
</tr>
<tr>
<td>HIV seropositive</td>
<td>441 (245–797)</td>
<td>–38.5 (–52.6 to –20.1)</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>HIV infected</td>
<td>385 (189–783)</td>
<td>–46.4 (–63.4 to –21.4)</td>
<td>...</td>
<td></td>
</tr>
<tr>
<td>Model 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV seronegative</td>
<td>1101 (662–1832)</td>
<td>Baseline</td>
<td>5.6 (5.0–6.4)</td>
<td>&lt;.001^d</td>
</tr>
<tr>
<td>HIV seropositive</td>
<td>426 (136–1334)</td>
<td>–61.3 (–79.4 to –27.2)</td>
<td>6.4 (4.8–9.3)</td>
<td>.002^e</td>
</tr>
<tr>
<td>HIV infected</td>
<td>159 (37–687)</td>
<td>–85.6 (–94.4 to –62.5)</td>
<td>8.5 (5.5–18.6)</td>
<td>.013^f</td>
</tr>
</tbody>
</table>

**NOTE.** The mean antimeasles virus antibody concentration at birth and the rate of decrease of passively acquired antimeasles virus antibodies were either similar or allowed to vary by HIV-1 exposure or infection status. See Methods for full description of models. GMC, geometric mean concentration.

^a Determined by the likelihood ratio test.

^b Model 2 versus model 1.

^c Model 3 versus model 1.

^d Model 4 versus model 1.

^e Model 4 versus model 2.

^f Model 4 versus model 3.

Naturalizing antibodies to MV were lower at birth in infants born to HIV-1–infected women than in infants born to uninfected women. This finding is consistent with data from a study in Kenya that found that the level of antibody to MV in umbilical cord blood samples was 35% (95% CI, 9.8–53.2) lower in infants born to HIV-infected women than in those born to HIV-uninfected women [7] and with data from a smaller study in Brazil that reported lower levels of antibodies to MV in umbilical cord blood samples from infants born to HIV-1–infected women than in infants born to HIV-uninfected women [5, 8]. These earlier studies used EIAs to measure levels of antibodies to MV. Our study is, to our knowledge, the first to measure antibody levels by the more sensitive plaque reduction neutralization assay [18].

Two possible mechanisms for lower levels of antibodies to MV at birth in infants born to HIV-1–infected women are low maternal antibody levels and/or impaired placental transfer [4]. Unfortunately, we were unable to assess the relative contributions of these mechanisms as determinants of infant measles serum antibody level during the prevaccination period, because maternal or umbilical cord blood samples were not obtained. In the Kenyan study, maternal HIV-1 infection was associated with a 16% reduction in the ratio of antibodies to MV in umbilical cord blood, compared with maternal blood, after adjusting for potential confounders [7]. In another study of Kenyan mothers and infants, maternal HIV-1 load during the third trimester of pregnancy was associated with reduced placental antibody transfer as measured by the ratio of antibodies to MV in umbilical cord blood, compared with that in maternal blood [19], although it is not clear whether HIV-1 load directly interferes with placental transfer or whether it is a marker of other immunopathologic characteristics. Other studies have similarly reported lower levels of antibodies to MV in HIV-1–infected adults than in uninfected adults [5, 7, 8, 20], although only 1 study reported a statistically significant decrease (P = .05) [20]. Differences in antibody levels between HIV-1–infected and HIV-uninfected Zambian women are unlikely to result from differences between women with vaccine-induced immunity and those with immunity following exposure to wild-type MV. Measles vaccine coverage in Zambia was estimated to be only 49% in 1984 [21] (the earliest available World Health Organization estimate). Therefore, most mothers in our study were likely to have been immune as a result of infection with circulating wild-type measles virus. In addition, we did not have
data on gestational age and were not able to exclude infants who were likely to have had low levels of passively acquired antibodies because of premature birth.

Among infants aged <7 months, the proportion with antibody levels $>120$ mIU/mL was lowest for HIV-1–infected infants, highest for HIV-seronegative infants, and intermediate for HIV-seropositive but uninfected infants at all ages. By 7 months of age, almost all infants were estimated to have antibody levels $<120$ mIU/mL. Our use of a cutoff value of 120 mIU/mL is based on the assumption that the levels of passively acquired antibody required for protection are similar to those of actively acquired antibody following vaccination [14]. This may be a simplistic assumption, because it ignores the role of memory and cellular immune responses in infants with active immunity; thus, susceptibility to MV may occur even earlier than shown in figure 2. The importance of cellular immunity to MV is suggested on the basis of the ability of infants with agammaglobulinemia to fully recover from measles, whereas infants with severe defects in T lymphocyte function often develop severe or fatal disease [22].

To our knowledge, this is the first published study of passively acquired antibodies to MV to confirm infant HIV-1 infection by detection of HIV-1 RNA, and differences in levels of passively acquired neutralizing antibodies to MV between HIV-1–infected infants and HIV-seropositive but uninfected infants have not been previously reported. Our findings suggest that HIV-1–infected infants are at particular risk of measles prior to the age of routine vaccination, even during the first 6 months of life.

Our data suggest that both the levels of passively acquired
antibody at birth and the rates of antibody level decrease differ among HIV-1–infected infants, HIV-seropositive but uninfected infants, and HIV-seronegative infants. Previous estimates of the half-life of passively acquired antibodies to MV ranged from 6.6 to 8.7 weeks [4]. Our findings are consistent with these estimates, as well as with estimates from other countries in sub-Saharan Africa, including Kenya (estimated half-life of passively acquired antibodies to MV, 6.6 weeks) [23] and Ghana (5.7 weeks) [24]. Perhaps surprisingly, the half-life of passively acquired antibodies to MV was estimated to be longest in HIV-1–infected infants and shortest in HIV-seronegative infants. HIV-1–infected infants were more likely to be malnourished and ill at the time of blood sampling; both of these factors would be expected to increase the catabolism of immunoglobulins. However, the absolute antibody levels in HIV-1–infected infants were much lower than those in HIV-1–uninfected infants. The rate of decrease of passively acquired antibody levels may be a function of the initial levels, with more rapid decrease rates in infants with the highest levels of passively acquired antibodies [25]. This may explain, in part, the differences in antibody kinetics that were seen between infants born with varying levels of passively acquired antibodies.

A large proportion of Zambian infants born to HIV-1–infected women had neutralizing antibody levels that would not interfere with vaccine responses several months before the age of routine measles vaccination. The World Health Organization has recommended that HIV-1–infected infants receive the first dose of measles vaccine at 6 months of age and the second dose at nine months of age [26], but this policy is difficult to implement, because the HIV-1 infection status of infants is usually not known in routine immunization programs, and under ideal conditions, severely immunocompromised HIV-1–infected infants should not receive measles vaccine [27]. Mass supplementary immunization campaigns have been successful in reducing MV transmission among all age groups in many developing countries [28] and may be especially important in countries with high HIV-1 prevalence to provide indirect protection to young HIV-1–infected infants who are susceptible to MV infection.

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Potential conflicts of interest. All authors: no conflicts.

References


