Persistence of Vaccine-Induced Measles Antibody Beyond Age 12 Months: A Comparison of Response to One and Two Doses of Edmonston-Zagreb Measles Vaccine Among HIV-Infected and Uninfected Children in Malawi

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Background. Previously, we demonstrated that measles antibody prevalence was lower at age 12 months among children infected with human immunodeficiency virus (HIV) than uninfected children following measles vaccination (MV) at ages 6 and 9 months. Among HIV-uninfected children, measles antibody prevalence was lower among 1- than 2-dose MV recipients. Here, we report results through age 24 months.

Methods. Children born to HIV-infected mothers received MV at 6 and 9 months, and children of HIV-uninfected mothers were randomized to MV at 6 and 9 months or MV at 9 months. We followed children through age 24 months. The child’s HIV status was determined and measles immunoglobulin G (IgG) level was measured by enzyme immunoassay (EIA) and by plaque reduction neutralization (PRN) on a subset.

Results. Among HIV-uninfected children, the difference in measles antibody prevalence at age 12 months between one- and two-dose recipients reported previously by EIA was shown to be smaller by PRN. By age 24 months, 84% and 87% of HIV-uninfected children receiving 1 or 2 doses, respectively, were seroprotected. Only 41% of 22 HIV-infected children were measles seroprotected at age 20 months.

Discussion. Measles seroprotection persisted through age 24 months among HIV-uninfected children who received 1 or 2 doses of MV. HIV-infected children demonstrated seroprotection through age 12 months, but this was not sustained.

Measles is listed among the leading causes of childhood mortality [1], although deaths due to measles infection have been dramatically reduced due to tremendous vaccination efforts [2]. Recent outbreaks in countries that had previously reached low measles incidence, however, demonstrate the need for sustained efforts [3]. Due to the highly infectious nature of measles, mathematical models predict that 90%–95% population immunity is needed to reduce measles transmission below the epidemic threshold [4]. To achieve such high population immunity, it is believed that 2 doses of measles vaccine (MV) are needed with >90% coverage of each dose [2].

In Africa, most countries administer a single dose of MV at age 9 months, complemented by mass vaccination of wider age groups in supplementary immunization activities (SIA). In 2009, the World Health Organization (WHO) and UNICEF estimated that the regional average coverage with the first dose of MV was 69%, well below the herd immunity threshold [5]. Africa also has the highest prevalence of HIV infection in the world [6]. Trans-placental transfer of maternal...
measles antibody is less efficient from HIV-infected mothers [7, 8]; thus HIV-infected infants may become susceptible to measles earlier in infancy than HIV-uninfected infants. The risk of death following measles is also higher in HIV-infected infants [8–10]. For these reasons, WHO states that infants living in areas with a high incidence of both HIV infection and measles, including those at high risk of developing measles before age 9 months, may receive the first dose of MV at age 6 months with 2 additional doses according to the national immunization schedule [2].

We previously studied the response to 2 doses of MV administered at ages 6 and 9 months (early 2-dose schedule) among children in Malawi with and without HIV infection, compared with HIV-uninfected children vaccinated with 1 dose of MV at age 9 months. In that study, we observed lower measles antibody prevalence at age 12 months among HIV-infected children compared with HIV-uninfected children immunized using either the 1- or 2-dose MV schedule. However, among HIV-uninfected children the seroprevalence of measles antibody was higher following the early 2-dose schedule than in children given a single dose at age 9 months [11]. This study provides follow-up through at least the second year of life and reports results on a subset of participants tested using a sensitive plaque reduction neutralization assay (PRN) for measles antibody.

**METHODS**

**Study Design**

Study methods were described elsewhere [11]. Briefly, from August 2000 to March 2002, mother-infant pairs were enrolled during the infants’ 14 week routine immunization visit at Ndirande Health Center near Blantyre, Malawi, an area of low measles incidence. A maternal blood sample was drawn for HIV and measles antibody testing, and baseline demographic information collected. Children of HIV-infected mothers were assigned to receive standard-titer Edmonston-Zagreb (Berna Biotech, formerly Swiss Serum and Vaccine Institute) measles vaccine (MV) at ages 6 and 9 months, and all other children were randomized to receive MV at either 6 and 9 months, 9 months only, or to receive MV at 9 months without follow-up. Blood was drawn and clinical information was collected during visits scheduled at ages 6, 9, 12, 20, 24, and for some, 30–36 months. Clinical information was also obtained on outpatient clinic visits, hospitalizations, and deaths. Antiretroviral therapy was not available in the public sector at the time of this study, and vitamin A was administered at ages 6 and 12 months, in accordance with country protocol. CD4 counts of the children were unavailable. Parents or guardians provided written informed consent for participation in the study. Ethical approval was obtained from the College of Medicine Research Committee in Malawi (University of Malawi), the London School of Hygiene and Tropical Medicine, and the Centers for Disease Control and Prevention (CDC). The protocol was reviewed by the World Health Organization (WHO) and the Malawi Ministry of Health.

In August of 2002, a nationwide measles vaccination SIA for children ages 9–59 months was conducted. Because of the low national incidence of measles (no measles was reported in Ndirande during the study period), the Institutional Review Boards and Ministry of Health approved that children in the measles study who were <20 months at the time of the campaign could be given the option to defer SIA vaccination until age 20–24 months. Children given an additional dose of vaccine in the campaign were excluded from analysis at the time of campaign vaccination.

**Measles and HIV Testing**

Measles antibody was tested at the CDC on all serum samples by EIA (Trinity Biotech) [11]. A subset of children was also tested at the Food and Drug Administration by a more sensitive PRN assay [12] including a random sample of children with follow-up through at least the 12 and 24 month study visits, respectively, to avoid any potential bias of only children who remained in the study to the end of follow-up. The sample sizes for the children in each of these three subsets were: 250 HIV-uninfected children vaccinated at 6 and 9 months, regardless of maternal HIV status, 250 HIV-uninfected children vaccinated at 9 months only (born to HIV-uninfected mothers), and all HIV-infected children (n = 72).

Specimen processing, HIV testing, and measles serologic testing by immunoglobulin G (IgG) enzyme immunoassay (EIA) have been described elsewhere [11]. Briefly, HIV-exposed children were tested using 2 commercially available rapid HIV-1 antibody assays with discrepant results between the assays confirmed by enzyme-linked immunosorbent assay or Western Blot. Samples from each study visit of HIV-antibody–positive children or children with samples unavailable after age 12 months were tested by real-time reverse transcriptase polymerase chain reaction [13].

PRN assays were conducted in duplicate on serum samples of children and mothers using 4-fold dilutions. A titer of 1:8 was equivalent to 8 mIU/mL and samples with a titer <1:8 were assigned a value of 4 mIU/mL when calculating geometric mean concentrations (GMC). All samples were run in parallel with the Second International WHO Serum Standard 66/202 (kindly provided by the National Institute for Biological Standards and Control, UK). Data were pooled from assays in which the end-point titer measured for the WHO reference serum did not vary by >20% from the assigned titer of 1:5000. The laboratory was blinded to study group assignment, and all samples related to a single child were tested on the same day. We define seropositivity as a positive result from the measles EIA and a seroprotective antibody titer as an antibody titer
$\geq 120$ mIU/mL determined by PRN; individuals with titers $<120$ mIU/mL were considered to be susceptible [14, 15].

Statistical Analysis

All single-dose recipients were HIV-uninfected. Among 2-dose recipients, children were classified in 3 groups: HIV-uninfected, HIV-exposed but uninfected, and HIV-infected children. Children with HIV seroconversion age $>12$ months were analyzed separately. Proportional differences in measles EIA or PRN responses between study groups were evaluated by $\chi^2$ test or the Fisher exact test. Comparisons of GMCs determined by PRN between groups at each visit were conducted using analysis of variance and adjustment for multiple comparisons by the Tukey-Kramer method. Demographic characteristics, loss to follow-up, and measles seropositivity were evaluated using $\chi^2$ tests and by multivariate logistic regression. Survival by group was assessed using Kaplan-Meyer survival curves and the Cox proportional hazards model. All analyses were performed using Stata software, version 8.0 (Stata) or SAS version 9.2 (SAS Institute).

RESULTS

Study Population

Of 2200 children enrolled and 1756 (80%) followed, a total of 1185 (66%) children remained in the study until the 12-month visit. Figure 1 shows the study participation rate at each visit by study group through ages 24–36 months. Study attrition occurred for several reasons, most frequently due to families moving out of the area, and occurred at equal frequency in the HIV-uninfected groups and HIV-exposed but uninfected group (range 11–13%). The survival rate was high among HIV-uninfected children enrolled in the study.
Characteristics significantly associated with loss to follow-up by age 20 months among the HIV-uninfected groups were having 4 or more children in the home, not owning the home, paternal education of less than secondary school, and low birth weight ($P < .01$) (data not shown). HIV-infected children had significantly higher attrition; 58 (68%) HIV-infected children were lost to follow-up by age 20 months, with mortality being the leading cause ($n = 34$, 59%).

### Demographics

The characteristics of children remaining in the study through ages 12 and 20 months did not differ significantly (Table 1). However, the sample size decreased significantly after the 20-month visit, largely due to revaccination during the measles vaccination campaign. There were no significant differences in demographic characteristics between study groups without HIV infection; however, HIV-infected children were significantly more likely to be underweight at birth (19%) and both underweight (58%) and wasted (weight-for-height measurement $>2$ standard deviations below the population mean) (15%) at age 20 months compared with HIV-uninfected children vaccinated at 9 months ($P < .001$). Children randomly selected for PRN testing were representative of their study groups (data not shown).

### Table 1. Demographic Characteristics of Children Remaining in the Study at Age 20 Months

<table>
<thead>
<tr>
<th>9-month Vaccination Group</th>
<th>6- and 9-month Vaccination Groups</th>
<th>HIV-infected mothers; HIV-infected children (N=26)</th>
<th>HIV-infected mothers; HIV-exposed but uninfected children (N=174)</th>
<th>HIV-negative mothers and children (N=447)</th>
<th>HIV-negative mothers and children (N=355)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>213 (47.7)</td>
<td>172 (48.5)</td>
<td>99 (56.9)</td>
<td>11 (42.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Does not own home</td>
<td>300 (67.1)</td>
<td>242 (68.2)</td>
<td>123 (70.7)</td>
<td>19 (73.1)</td>
<td>NS</td>
</tr>
<tr>
<td>&gt;4 kids in the home</td>
<td>94 (21.0)</td>
<td>52 (14.7)</td>
<td>24 (13.8)</td>
<td>2 (7.7)</td>
<td>NS</td>
</tr>
<tr>
<td>No electricity in home</td>
<td>273 (61.1)</td>
<td>203 (57.2)</td>
<td>104 (59.8)</td>
<td>16 (61.5)</td>
<td>NS</td>
</tr>
<tr>
<td>No running water in home</td>
<td>422 (94.4)</td>
<td>340 (95.8)</td>
<td>165 (94.8)</td>
<td>23 (88.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Maternal Education &gt;Primary</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paternal Education &gt;Primary</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth weight &lt;3.0 kg</td>
<td>235 (52.6)</td>
<td>181 (51.0)</td>
<td>101 (58.1)</td>
<td>18 (69.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Stunted</td>
<td>89 (20.5)</td>
<td>79 (22.4)</td>
<td>44 (26.0)</td>
<td>9 (34.6)</td>
<td>&lt;.1</td>
</tr>
<tr>
<td>Underweight</td>
<td>14 (3.2)</td>
<td>15 (4.3)</td>
<td>10 (5.9)</td>
<td>5 (19.2)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Wasting</td>
<td>4 (0.9)</td>
<td>2 (0.6)</td>
<td>4 (2.4)</td>
<td>1 (3.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Nutritional status at 18 months of age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stunted</td>
<td>289 (73.2)</td>
<td>238 (74.1)</td>
<td>111 (70.3)</td>
<td>22 (84.6)</td>
<td>&lt;.1</td>
</tr>
<tr>
<td>Underweight</td>
<td>90 (22.8)</td>
<td>69 (21.5)</td>
<td>40 (25.3)</td>
<td>15 (57.7)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Wasting</td>
<td>5 (1.3)</td>
<td>7 (2.2)</td>
<td>0 (0.0)</td>
<td>4 (15.4)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

**NOTE.** a No significant (NS) differences between HIV-uninfected groups were detected. NS indicates $P > .1$. 

b Denominator may differ slightly as birthweight data was not available for all children.
Measles EIA Antibody

Table 2 shows the proportion of children with measles antibody detected by EIA at each study visit. By age 20 months, there were no statistically significant differences between HIV-uninfected groups; ~81% of single-dose recipients and 77%–83% of 2-dose recipients among HIV-exposed and unexposed, respectively, were measles seropositive. Among HIV-infected children, only 44% of 23 children (95% CI, 23%–63%) were measles positive at age 20 months. Measles seropositivity at age 24 months was slightly lower than at age 20 months among HIV-unexposed children (84% and 90%, respectively), while among HIV-exposed but uninfected children it had fallen from 83% of 114 to 69% of 42 children. None of the 3 remaining HIV-infected children in the study had demonstrable measles antibody by EIA.

Measles PRN Antibody GMCs

Among HIV-uninfected children, there were differences between groups in the GMCs at age 12 months but these differences narrowed substantially by the 20 and 24 month specimens (Figure 3). At the 9-month visit following 6-month vaccination, the calculated GMC for the three groups who received MV at age 6 months ranged from 130 to 176 mIU/mL, above the level considered to be protective. After all study children had received 1 or 2 doses of MV, the GMC at the 12-month visit was significantly lower among the single-dose group (P < .001) than among 2-dose HIV-uninfected recipients, and comparable to HIV-infected children who had received 2 doses. However, at the 20-month visit, the GMC among single-dose recipients had increased to 511 mIU/mL, higher than all other study groups. By the 24-month visit, there appeared to be a decrease in antibody levels for all of the vaccine groups, though not statistically significant. Regardless of vaccination schedule, all HIV-uninfected children at the 24-month visit demonstrated a GMC within a comparable range (318–401 mIU/mL) with no statistical differences between groups. Only 6 HIV-uninfected and no HIV-infected children were tested at age 30 months, and no further declines in GMC were observed (data not shown).

HIV Seroconverters After Age 12 Months

Ten children who seroconverted to HIV at >12 months of age had responses to measles vaccine comparable to those seen in HIV-uninfected children also vaccinated at 6 and 9 months. One was excluded from analysis due to receipt of vaccination outside of the study clinic. Of the remaining 9 subjects, 89% were measles seropositive by EIA at age 12 months with a corresponding GMC of 339 mIU/mL. Significant differences were found in the proportion positive by EIA compared with PRN at the 12 and 20 month visits among HIV-uninfected children vaccinated at age 9 months and at the 24 month visit among HIV-exposed, but uninfected children vaccinated at ages 6 and 9 months.

### Table 2. Measles Seroprotection Rates by Plaque Reduction Neutralization (PRN) and Seropositive Rates by Enzyme Immunoassay (EIA), According to Vaccination Schedule and HIV Infection Status Among Children in Malawi.

<table>
<thead>
<tr>
<th>Study Visit</th>
<th>9-month Vaccination Group</th>
<th>6- and 9-month Vaccination Groups</th>
<th>HIV-infected mothers; HIV-infected children</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV-negative mothers and children</td>
<td>HIV-negative mothers; HIV-exposed, but uninfected children</td>
<td>HIV-infected mothers; HIV-infected children</td>
</tr>
<tr>
<td>EIA Results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>no.</td>
<td>%</td>
<td>no.</td>
</tr>
<tr>
<td>6 month visit</td>
<td>–</td>
<td>–</td>
<td>165</td>
</tr>
<tr>
<td>9 month visit</td>
<td>158</td>
<td>6</td>
<td>85</td>
</tr>
<tr>
<td>12 month visit</td>
<td>158</td>
<td>6</td>
<td>83</td>
</tr>
<tr>
<td>20 month visit</td>
<td>162</td>
<td>9</td>
<td>84</td>
</tr>
<tr>
<td>24 month visit</td>
<td>86</td>
<td>0</td>
<td>48</td>
</tr>
<tr>
<td>PRN Results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>no.</td>
<td>%</td>
<td>no.</td>
</tr>
<tr>
<td>6 month visit</td>
<td>–</td>
<td>–</td>
<td>158</td>
</tr>
<tr>
<td>9 month visit</td>
<td>158</td>
<td>6</td>
<td>83</td>
</tr>
<tr>
<td>12 month visit</td>
<td>158</td>
<td>6</td>
<td>84</td>
</tr>
<tr>
<td>20 month visit</td>
<td>162</td>
<td>9</td>
<td>84</td>
</tr>
<tr>
<td>24 month visit</td>
<td>86</td>
<td>0</td>
<td>48</td>
</tr>
</tbody>
</table>

Note. a Statistically significant comparison with the 9-month vaccination group.
b Statistically significant comparison with the HIV-infected children.
c Statistically significant comparison with HIV-exposed, but uninfected children.

Note: Seroprotection by PRN defined as a titer >120 mIU/mL. Significant differences were found in the proportion positive by EIA compared with PRN at the 12 and 20 month visits among HIV-uninfected children vaccinated at age 9 months and at the 24 month visit among HIV-exposed, but uninfected children vaccinated at ages 6 and 9 months.
Comparison of PRN and EIA Measles Antibody Seroprevalence

For maternal samples and children’s samples at ages 6 and 9 months, the measles seropositivity rates were comparable between assays (Table 2). The proportion of children seropositive by PRN was higher than by EIA in most instances, but the differences were only statistically significant at the 12- and 20-month visits among children vaccinated at 9 months only (\( P < .01 \)) and at the 24-month visit for HIV-exposed but uninfected vaccinated at 6 and 9 months (\( P < .01 \)).

The sensitivity and specificity of the EIA was compared with the PRN, using 2344 specimens from all study groups and visit times that were tested by both assays. The sensitivity of the EIA was 1412/1547 (91% [95% CI, 90%–92%]) and the specificity was 727/797 (91% [95% CI, 90%–92%]). The HIV-infection status of the mother or child did not have an apparent effect on the sensitivity or specificity of the EIA. In a scatter plot of EIA OD values against PRN measles antibody titer, there appeared to be a linear relationship (Figure 4).

Loss of Detectable Measles Antibody

Among 2-dose recipients, HIV infection (OR 5.0, 95% CI, 2.0–12.4, \( P < .001 \)) and male sex (OR 2.6, 95% CI, 1.4–4.6, \( P < .01 \)) were associated with lack of detectable measles EIA antibody by age 20 months. In children who were measles EIA positive at age 12 months, 112 (13%) of 751 children had no detectable EIA antibody in the 20- or 24-month specimen. Children given a single dose of MV at age 9 months were least likely to lose detectable antibody (6%) between 12 and 20–24 months. With the single-dose group as reference, loss of detectable measles EIA antibody was significantly more common in the other groups: HIV-uninfected children vaccinated at 6 and 9 months (16%; OR 5.2 [95% CI 1.7–14.7]), HIV-uninfected but exposed children (13%; OR = 3.0 [95% CI 1.7–5.3]) or HIV-infected children (27%; OR = 6.6 [95% CI 2.6–16.8]). Males were 1.7 times more likely to lose detectable antibody by measles EIA (\( P < .05 \), 95% CI 1.1–2.5), and HIV-infected children were 2.3 times more likely to lose detectable antibody when compared with all other children vaccinated at 6 and 9 months (\( P < .001 \), 95% CI 1.57–3.46).

The proportion of study children with a loss of measles antibody was lower by PRN than by EIA. Among 291 children with titers >120 mIU/mL at 12 months and with specimens tested at age 20 or 24 months, 30 (10%) lost protective antibody levels. This was more common among 2-dose (11%) than 1-dose (7%) HIV-uninfected recipients, though not a statistically significant difference, and was highest (36%) among HIV-infected children (\( P < .001 \) using 1-dose HIV-uninfected recipients as the reference group).
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DISCUSSION

In HIV-uninfected children, early 2-dose measles vaccination at age 6 and 9 months provided some protection under age 9 months while achieving a similar rate of protection at age 24 months as a single dose administered at age 9-months. These findings complement our previous study, which demonstrated that >90% of HIV-uninfected vaccinees immunized using an early 2-dose schedule were seropositive through age 12 months when tested by EIA without any detectable increase in serious adverse events [11]. In this study, by age 24 months, 84% and 87% of HIV-uninfected children vaccinated at age 9 months and at age 6 and 9 months, respectively, demonstrated protective levels of measles antibodies by PRN. Both the EIA and PRN findings support the WHO recommendation for an early 2-dose schedule (at 6 and 9 months) for young children at high risk for measles infection, for example, during a measles outbreak [16].

Among HIV-infected children, however, the early 2-dose schedule did not provide lasting immunity. Although these children had similar seropositivity rates after the first dose of vaccine administered at age 6 months as HIV-uninfected children, they did not show a high increase in titer following the second dose (GMC = 206), and by age 12 months, as reported previously, the proportion measles seropositive was lower than among HIV-uninfected children [17]. In addition, the proportion of HIV-infected children measles antibody positive by PRN at age 12 months after 2 doses of vaccine in our study (69%) was lower than the 88% of HIV-infected children aged 15 months reported in Lusaka, Zambia after a single dose of the same MV at age 9 months [17]. Thus it appears that early 2-dose vaccination of HIV-infected children did not provide more lasting protection than vaccination at age 9 months, although direct comparison between the 2 studies is hindered by the ongoing measles transmission in Lusaka at the time of the Zambian study. In both studies, antibody levels decreased rapidly in HIV-infected children, consistent with earlier studies that showed rapid waning [18, 19] and a median half-life of vaccine-induced antibodies of 18 months [20].

Unfortunately, we did not obtain CD4 cell counts and HIV viral loads; thus, immune suppression could not be determined directly. Further study will be needed to understand the effect of highly active antiretroviral therapy (HAART) on response to immunity from measles vaccination in developing countries; however, recent data demonstrate that receipt of measles vaccine following immune recovery due to HAART can result in persistent measles antibody production [21]. In addition, we have not evaluated the impact of revaccination of HIV-infected children during the SIA.

The difference in measles EIA antibody response among HIV-uninfected children at age 12 months between 1- and 2-dose recipients previously reported [10] was diminished when samples were assayed by the more sensitive PRN assay (Table 2). Moreover, by age 24 months, the measles seropositivity rate and GMCs for the 2 groups were comparable, and consistent with antibody levels at age 24 months in HIV-uninfected, single-dose recipients reported from Zambia (451 mIU/mL [95% CI 382–529]) [17]. A similar pattern was found in children born to mothers in North America with vaccine-derived immunity when measles antibody titers for children vaccinated at ages 6 and 15 months were compared with those vaccinated once at age 15 months [22]. The kinetics of the response in our study, however, seemed different for those vaccinated at 6 and 9 months versus those vaccinated at 9 months only (Figure 3). For children given vaccine at 6 and 9 months, PRN titers appeared to peak at age 12 months and then declined by 20–24 months. By contrast, the 9 month group had the highest GMCs at age 20 months. However, the study design was not optimized to capture peak responses to vaccination and may have underestimated responses and maximal GMCs in each group.

We confirmed that PRN testing was more sensitive than EIA, consistent with studies that have indicated that EIA assays are less sensitive in serum specimens with lower measles antibody titers (ie,  500 mIU/mL) [15, 23]. Among single-dose vaccine recipients tested at ages 12 and 20 months, the percent seropositive was significantly lower by EIA than by PRN. Nonetheless, the pattern of changes over time in percentage measles seropositive was similar whether antibody was measured by EIA or PRN, and the specificity of the EIA assay was high. EIA can be a practical and useful measure of measles seroresponse, but if groups under comparison have low measles antibody levels, differences observed by EIA should ideally be confirmed by the more sensitive PRN assay.

In contrast to HIV-infected children, the measles PRN and EIA seropositivity rates among HIV-infected mothers in this study were comparable to those seen in HIV-uninfected mothers.
(Figure 3). This is consistent with the high seropositivity rates reported in HIV-infected adults in the United States, suggesting that persons with measles immunity prior to contracting HIV maintain that immunity [24–26]. Although our sample size was small, the 10 children who developed HIV infection after a year of age had similarly high rates of measles positivity.

Interestingly, HIV-exposed but uninfected children had the highest response rate to the first dose of MV determined by both EIA and PRN, although not a statistically significant difference. It has been shown that HIV-infected mothers may transfer less measles antibody [7] and antibody of lower avidity [18] through the placental barrier, thus reducing maternal antibody interference. And although the EZ vaccine, such as that used in our study, has been found to induce greater seroresponsiveness than Schwarz vaccine in the presence of maternal antibody [27], maternal antibody over 50–100 mIU/mL reduced seroresponses to standard titer EZ vaccines [28, 29]. We did not evaluate maternal transfer of measles antibodies, but our prevaccination results by PRN showed that none of the HIV-exposed, but uninfected children had measles neutralizing antibody titers >120 mIU/mL compared with 6% of HIV-unexposed children.

This study supports the WHO recommendations for measles vaccination beginning as early as age 6 months followed by 2 additional doses in areas with a high incidence of both HIV infection and measles, although protection may be short-lived in HIV-infected children. Fortunately, accelerated measles control and elimination activities have proven to be successful even in areas of high HIV prevalence [30]. Furthermore, the distribution of antiretroviral therapy has greatly reduced rates of maternal-child transmission of HIV [31]. While additional data on the response and duration of protection from measles vaccination of HIV-infected children on antiviral therapy will be of interest, the priority for measles control is to implement and sustain known effective strategies in all countries.

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