Long-term Immune Responses to Vaccination in HIV-Infected Patients: A Systematic Review and Meta-Analysis

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Vaccine-induced antibodies may wane more quickly in persons living with human immunodeficiency virus (HIV) than in healthy individuals. We reviewed the literature on vaccines routinely recommended in HIV-infected patients to estimate how seroprotection decreases over time in those who initially responded to immunization. For each study retrieved from the literature, the decrease of seroprotection was modeled with a log binomial generalized linear model, and data were pooled in a meta-analysis to provide estimates of seroprotection 2 and 5 years after the last vaccine administration. Our analyses confirmed that the duration of seroprotection was shorter in HIV-infected patients and that with current guidelines, a substantial proportion of patients would have lost protective antibodies before a booster was proposed. We therefore discuss the implications for the monitoring of antibody levels and timing of revaccination in these patients.

Keywords. vaccination; HIV; meta-analysis.

Immune responses to most vaccines are known to be impaired in patients with human immunodeficiency virus (HIV) infection [1, 2]. However, besides the primary response, long-term persistence of protection has been poorly documented. As of today, recommendations on the timing of booster injections were based on data collected in healthy persons, although antibody decay patterns may be different. In this respect, an important step is to estimate how seroprotection decreases over time among patients who initially responded to immunization. In the current study, we reviewed data on long-term persistence of antibody concentrations after vaccination in HIV-infected patients. There were 3 main reasons for this choice: (1) antibody concentrations are reported in most vaccine trials, providing enough data to allow meta-analysis; (2) correlates of protections have been defined for most vaccines; and (3) antibody levels for most antigens can be routinely assessed with standardized methods. For some vaccines (ie, measles, varicella, and yellow fever), cell-mediated immunity is the critical determinant of protection; however, methods for evaluating cellular responses are not easily comparable between studies, and correlates of protection not yet established. Our goal here was to provide a summary of available data to guide recommendations on revaccination in HIV-infected persons.

METHODS

Search Strategy and Selection Criteria
Using PubMed, we searched the MEDLINE database for English-language articles up to January 2013, without date restriction, using the terms vaccine, antibodies, follow-up, long-term, decline, duration, and HIV (see search equation in the Supplementary material). The
review and meta-analysis were conducted according to the PRISMA guidelines. Studies were selected by 1 author (S. K.) according to the eligibility criteria: original experimental or observational studies on licensed vaccines in patients living with HIV, reporting measurements of antibody titers beyond 6 months after the last vaccine dose administration. Reports on influenza vaccines were excluded. The reference lists of all relevant articles were examined for additional data sources.

For each article, we abstracted the study design, vaccination protocols, sample size, follow-up duration and the percentage of “primary responders” (patients who had mounted protective antibody titers after immunization) who remained seroprotected over time. Protective levels defining seroprotection were those reported by the authors and are detailed in the Supplementary Information. Where relevant, the percentages of seroprotected patients were pooled in a meta-analysis. The meta-analysis was restricted to prospective studies and to vaccine antigens for which ≥2 studies were available. No meta-analysis was undertaken for pneumococcal vaccines because the specific antibody levels necessary for adequate protection against pneumococcal disease are not clearly defined, even in healthy persons [3].

Data Analysis
To account for the great heterogeneity in follow-up times between the different studies, we first modeled for each study the decrease in seroprotection $P(t)$, as a function of time since immunization, as $P(t) = \exp(-\beta t)$, where $\exp(-\beta)$ was the relative decrease in protection per additional time unit ($t$) since immunization. Data were fit using log binomial generalized linear models. The predicted percentages of seroprotected individuals 2 and 5 years after immunization in each study were then pooled in a meta-analysis with random effects and presented in forest plots. All analyses were made using R software, version 2.13.2 (R Development Core Team, R Foundation for Statistical Computing; http://www.r-project.org).

RESULTS
Of the 159 potentially relevant studies, 54 were selected for the qualitative review (Figure 1). For each vaccine, percentages of seroprotection retrieved from the literature are presented in Figure 2. Median follow-up ranged from 9 months to 9 years after the last vaccine dose. The median number of patients per study was 40 (interquartile range, 18–63). Data were available for 13 vaccine antigens: *Streptococcus pneumoniae* (n = 14), hepatitis B (n = 12), measles (n = 12), hepatitis A (n = 5), tetanus (n = 8), yellow fever (n = 3), *Haemophilus influenzae* type b (n = 3), rubella (n = 2), varicella (n = 1), pertussis (n = 1), poliovirus (n = 1), mumps (n = 1), and Japanese encephalitis (n = 1). Of the 54 studies included in the review, 19 fit the eligibility criteria for meta-analysis. Others were excluded because they were studies of pneumococcal vaccine (n = 14), were retrospective (n = 13), did not differentiate between outcomes in primary responders and nonresponders during follow-up (n = 4), or were the only study available for the vaccine (n = 4; pertussis [4], *H. influenzae* type b [5], varicella [6], and Japanese encephalitis [7]).

**Hepatitis B**
Twelve studies were included, with follow-up times ranging from 12 to 115 months [8–19]. As illustrated in Figure 2A, seroprotection typically decreased over time: after 3 40-µg doses of hepatitis B surface antigen (HBsAg), 71% of primary responders maintained protective antibody titers at year 1 [8], 33%–61% at year 2 [8, 10], and 40% at year 5 [10]. There was no clear trend of longer persistence of seroprotection with high-dose vaccination protocols [8, 10]. Three retrospective studies reported data beyond 5 years after immunization [11, 15, 19] in HIV-infected children born to HBsAg-positive HIV-infected mothers, and maintenance of seroprotection was particularly poor: 24% after 5.5 years [11], 45% after 8 years [15], to only 1% after 9.6 years [19] after 3 10-µg doses.

According to the meta-analysis, less than half of primary responders would maintain protective antibody titers 2 years after immunization (38%; 95% confidence interval [CI], 23%–54%) in adults and 61% (27%–90%) in children) and only 17% (3%–36%) after 5 years (Figures 3 and 4). Double-dosed vaccination protocols did not improve maintenance of seroprotection compared with standard doses of vaccine (41% [95% CI, 14%–71%] and 50% [24%–77%], respectively, after 2 years; $P = .65$).

**Hepatitis A**
We identified 1 retrospective [20] and 4 prospective [21–24] studies on hepatitis A. In adults, a slight decrease was observed over time (Figure 2B); 100% of responders were still seroprotected after 1 year [23], 90% after 3 years [21], and 85% after 4 years [22]. No data were reported beyond 4 years. In children, persistence of responses was lower: 85% (n = 84) after 9 months [20] and 92% after 18 months [24]. Percentages of seroprotection were not greater with 3-dose schedules [22, 23], compared with standard 2-dose schedules [21–24]. The pooled percentages of seroprotection against hepatitis A were 92% (95% CI, 89%–95%) after 2 years and 82% (76%–88%) after 5 years (Figures 3 and 4).

**Measles, Mumps, and Rubella**
Data on long-term persistence of measles immunity were reported in 12 studies, in children (n = 10) [25–34] or adults (n = 2) [35, 36]. As illustrated on Figure 2C, percentages of seroprotection varied widely between studies, reflecting the great heterogeneity in the populations studied. In sub-Saharan African children vertically infected with HIV, not receiving highly
active antiretroviral therapy (HAART), and vaccinated in the first months of life, percentages of seroprotection rapidly dropped during follow-up; 62%–73% of primary responders were still protected after 15 months [29, 31], 41%–49% after 28 months [25, 31], and 30% after 50 months [28]. HAART improved seroprotection, either for children started on HAART after immunization (69% after 6 months of HAART [28] 40%–60% after 4 to 7 years of HAART [26, 34]) or those who

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram of the search strategy. Abbreviation: HIV, human immunodeficiency virus.
were vaccinated or revaccinated after the start of HAART (73% after 1 year [30], 40%–82% after 4 years [32]). In the last study, higher percentages of seroprotection were reported 4 years after vaccination in children started on HAART in their first year of life (82%) than in others (40%) [32].

In adults, data were scarce and showed conflicting results. In studies conducted during childhood before HIV infection, 95% still had protective antibody titers at a median age of 35 years (n = 59) [36], whereas after revaccination of 26 HIV-infected adults at age 31 years, only 43% were still above the detection level after 1 year [35].

Because of great heterogeneity, the meta-analysis was restricted to 5 studies focusing on children vertically infected with HIV [26, 27, 29–31] and immunized at 6–42 months, with either 1 dose [31] or 2 doses [26, 27, 29, 30] of the measles-mumps-rubella vaccine. The pooled analysis estimated that in this particular population, protective antibody levels would persist in 68% (95% CI, 45%–88%) of primary responders after 2 years, and 40% (10%–73%) after 5 years (Figure 3C).

Only 3 studies reported data on rubella [26, 34] or mumps [26]. After 4 years of HAART, antibodies against mumps persisted in 62% of children and antibodies against rubella in 27%–89%, with the highest seroprotection rates reported for children with a virologic response.

**Tetanus, Poliomyelitis, and Pertussis**

Studies on tetanus included 241 children followed up from 12 to 53 months after immunization (Figure 2E) [28, 30, 32–34, 37–39]. Retrospective studies accounted for 76% of participants (n = 182). Percentages of seroprotection were high: 67%–90% within the first 2 years [30, 33, 34, 37–39] and 78% after 4 years [28]. Meta-analysis of the 4 prospective studies estimated overall percentages of seroprotection (Figure 3D) of 74% (95% CI, 57%–87%) and 43% (21%–66%) 2 and 5 years after immunization, respectively. One study each reported data on immunization against poliovirus [37], pertussis [4], and diphtheria [34]. In all reports, the duration of seroprotection was shorter than in healthy children.

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**Figure 2.** Data retrieved from the literature (A–F) and graphic illustration of the statistical modeling for hepatitis B (F). Each symbol represents a percentage of individuals with protective antibody concentrations in relation to time elapsed since immunization, among those who initially responded to the vaccine, except for tetanus vaccine, for which overall percentages of seroprotection are presented (responders and nonresponders pooled together). The sizes of points are proportional to the sample sizes of studies; symbols are color coded according to the vaccination protocol. F, Principle of modeling for hepatitis B vaccine. Symbols represent percentages of seroprotection retrieved from the literature, and lines show extrapolations of the model at 2 and 5 years. Estimates of seroprotection (black symbols) are provided by the model at 2 and 5 years.
Figure 3. Meta-analysis of the percentages of seroprotection 2 years after the last vaccine dose, by vaccine antigen. Columns on right detail characteristics of study participants at the time of immunization, including mean or median age, percentage receiving highly active antiretroviral therapy (HAART), mean or median CD4 cell count (per microliter), mean or median human immunodeficiency virus (HIV) load (log copies per milliliter), and percentage with undetectable HIV loads. Colors represent vaccination protocols. For hepatitis B, yellow symbols represent 3 intramuscular 10-µg doses (Lao–Araya et al [13] and Scolfaro et al [18]) or 3 subcutaneous 5-µg doses (Mannucci et al [14]) in children or 3 intramuscular 20-µg doses in adults (Kaech et al [12] and Rey et al [17]). Red symbols represent 3 intramuscular 40-µg doses (Cooper et al [10] and Cruciani et al [8]). Heterogeneity: Q = 121.9; P < .001; I² = 95% [92%–97%]. For hepatitis A, yellow symbols represent 1 dose (Weinberg et al [24], Crum-Cianflone et al [21], Kernéis et al [22], and Launay et al [23]); red symbols, 2 doses (Kernéis et al [22] and Launay et al [23]). Heterogeneity: Q = 2.9; P = .71; I² = 0% [0%–0%]. For measles, yellow symbols represent 1 dose (Moss et al [31]); red symbols, 2 doses (Moss et al [31]); red symbols, 2 doses (Melvin and Mohan [30], Bekker et al [26], Brunell et al [27], and Fowlkes et al [29]). Heterogeneity: Q = 25.6; P < .001; I² = 84% [65%–93%]. For tetanus, yellow symbols represent 2–5 doses plus boosters, according to local practices. Heterogeneity: Q = 2.5; P = .48; I² = 0% [0%–81.3%].

Abbreviations: CI, confidence interval; CV, Charge Virale (viral load); HAART, highly active antiretroviral therapy; Und., undetectable.
Figure 4. Meta-analysis of the percentages of seroprotection 5 years after the last vaccine dose, by vaccine antigen. Columns on right detail characteristics of study participants at the time of immunization, including mean or median age, percentage receiving highly active antiretroviral therapy (HAART), mean or median CD4 cell count (per microliter), mean or median human immunodeficiency virus (HIV) load (log copies per milliliter), and percentage with undetectable HIV loads. Colors represent vaccination protocols. For hepatitis B, yellow symbols represent 3 intramuscular 10-µg doses (Lao-Araya et al [13] and Scelfaro et al [18]) or 3 subcutaneous 5-µg doses (Mannucci et al [14]) in children or 3 intramuscular 20-µg doses in adults (Kaech et al [12] and Rey et al [17]). Red symbols represent 3 intramuscular 40-µg doses (Cooper et al [10] and Cruciani et al [8]). Heterogeneity: $Q = 87.7; P < .001; I^2 = 93\% [88\%–96\%]$. For hepatitis A, yellow symbols represent 1 dose (Weinberg et al [24], Crum-Cianflone et al [21], Kernéis et al [22], and Launay et al [23]); red symbols, 2 doses (Kernéis et al [22] and Launay et al [23]); heterogeneity: $Q = 6.7; P = .25; I^2 = 25\% [0\%–69\%]$. For measles, yellow symbols represent 1 dose (Moss et al [31]); red symbols, 2 doses (Melvin and Mohan [30], Bekker et al [28], Brunell et al [27], and Fowlkes et al [29]). Heterogeneity: $Q = 47.8; P < .001; I^2 = 92\% [84\%–96\%]$. For tetanus, yellow symbols represent 2–5 doses plus boosters, according to local practices. Heterogeneity: $Q = 4.5; P = .22; I^2 = 33\% [0\%–76\%]$. Abbreviations: CI, confidence interval; CV, Charge Virale (viral load); HAART, highly active antiretroviral therapy; Und., undetectable.
**S. pneumoniae**

All 14 studies on persistence of antibodies against *S. pneumoniae* were prospective, in either children (n = 5) [40–44] or adults (n = 9) [45–53] and involving a pneumococcal conjugate vaccine (PCV; n = 6) [40–44, 49] or the 23-valent pneumococcal polysaccharide vaccine (PPSV23; n = 9) [45–48, 50–53]. Follow-up ranged from 8 to 60 months after immunization (median, 12 months). The median number of patients was 33. The definition of response varied greatly between studies: a ≥2-fold increase in antibody titers [47, 49]; antibody concentrations above 0.35 µg/mL [42, 43, 47], 0.5 µg/mL [40], or 1 µg/mL [40, 41, 48, 49, 52]; or based on geometric mean titers alone [44–47, 49, 50]. After PPSV23 vaccination in adults, rates of decrease in antibody concentrations were either similar [45, 48, 52, 53] or more rapid [46, 50] compared with those observed in healthy individuals. Beyond 5 years, [47, 48], antibody concentrations had dropped below the cutoff values for most serotypes. This was reportedly more frequent in patients with low CD4 cell counts at vaccination or those who failed to achieve virologic suppression [47]. Vaccination with PCV was not directly compared with PPSV23 vaccination in adults, but 2 doses of 7-valent PCV elicited more sustained responses than 1 dose during the 1-year-follow-up [49].

In HIV-infected children, the immunogenicity of PCV has been assessed from 8 months to 5 years after primary immunization [40–44]. Here again, results were variable: HIV-infected children reportedly experienced a significantly greater decline in antibody levels during follow-up than HIV-uninfected children [42–44]; however, with a vaccination protocol including 2 PCVs and 1 PPSV23 at 8-week intervals, Abzug et al [40] showed that 22 months after immunization, decline in antibody concentrations were similar to those in HIV-uninfected infants after PCV alone.

**Other Antigens**

After immunization against *H. influenzae* b, estimates of seroprotection ranged from 16% to 78% [5, 30, 54] in children with vertical HIV infection at different time points after immunization. In the only report on varicella vaccine, <50% of 94 HIV-infected children (aged 1–8 years) still had detectable varicella zoster virus immunoglobulin G 1 year after the start of immunization [6]. For yellow fever, results of 3 retrospective studies [55–57] suggested that immunogenicity of yellow fever immunization waned more quickly in HIV-infected patients; the proportion of patients with nonreactive titers increased from 17% to 23% during the 10-year period after vaccination [57]. In the single study on an inactivated Japanese encephalitis vaccine in 50 HIV-infected children receiving HAART, only 4 of 38 primary responders lost protective antibodies during the 3-year follow-up, suggesting long-term benefit of the vaccination in this population [7].

**DISCUSSION**

The duration of seroprotection, as assessed by quantitative measurement of antibody responses, is shorter in HIV-infected patients than in otherwise healthy persons for most licensed vaccines. As a comparison, 65%–95% of healthy children and 80% of adults maintain protective concentrations of anti-hepatitis B virus antibodies 10 years after vaccination. With inactivated hepatitis A vaccine, mathematical models estimate that protective levels of anti–hepatitis A virus antibodies could be present for >25 years in adults and 14–20 years in children. Percentages of seroprotection reach 93%–10% in healthy children 10 years after tetanus vaccine and 95%–100% after measles vaccine (see references in Table 2 of the Supplementary material).

Our analyses showed a rapid decrease in seroprotection after immunization in HIV-infected patients and have several implications:

- Because of the high prevalence and severity of chronic hepatitis B in HIV-infected patients, it seems that anti–HBs virus antibodies should be measured yearly in adults and every 2–5 years in children at risk (those in close contact with HBsAg-positive persons or living in a high-endemicity country). Closer monitoring anti–HBs virus antibody titers could be considered in those with the lowest antibody titers at the end of the vaccination course (10–100 IU).
- For persons at increased risk for hepatitis A (ie, travelers, men who have sex with men, users of drugs, persons with occupational risk for hepatitis A virus infection or chronic liver disease), anti–hepatitis A virus antibodies should be monitored every 5 years since almost 20% of primary responders would have lost seroprotection by year 5 after immunization.
- For tetanus, the meta-analysis of prospective studies found that about 75% of HIV-infected children would maintain protective concentrations after 2 years, and retrospective studies found percentages of seroprotection of about 70%–80% after 5 years. In this respect, the interval of 10 years between boosters seems reasonable.
- To improve maintenance of seroprotection against measles, the initial vaccination should include 2 doses, ideally administered after the start of HAART, in children with undetectable viral loads. In children vaccinated before the start of HAART and/or with detectable HIV loads at the time of immunization, a third dose could be proposed 2–5 years after primary vaccination, when the CD4 cell count is >200 or >15% per microliter.
- The World Health Organization recently stated that a single dose of yellow fever vaccine was sufficient to confer life-long immunity against the disease in immunocompetent persons. Data show that immunity wanes more quickly in HIV-infected persons. In these patients, determination of antibody titers

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should be considered in case of potential exposure, and revaccination proposed to those with negative titers.

- For now, data on immunogenicity of PCV or strategies combining PCV and PPSV23 are too preliminary to allow statements on the optimal timing of booster injections in adults.

Several methodologic issues warrant discussion. First, it is remarkable that the median number of patients per study was only 40. Data on immunogenicity of vaccines in the immunocompromised host are scarce, and the small samples in each category gave little power for comparisons between age classes or vaccine protocols. Second, only prospective studies were included in the meta-analysis, which may have lead to a certain degree of underestimation of seroprotection. Indeed, as illustrated for tetanus, studies pooled in the meta-analysis were those with the shortest duration of follow-up and lower percentages of seroprotection. This choice, however, was essential to guarantee the quality of data analyzed. Conversely, relying on the exponential decrease could lead to overestimate the decrease in seroprotection. The choice of the model was supported by the good fit in studies in which ≥2 follow-up points were available (see Supplementary material). This model, however, leads by structure to an always decreasing trend in seroprotection with time, implying that all vaccinees will lose seroprotection at some point. An alternative assumption would be that some individuals would remain seroprotected permanently over time, as it has been hypothesized, for example, with hepatitis A vaccine.

There was also great heterogeneity in some important variables that complicated comparisons across studies: immunologic status at the time of vaccination, use of antiretroviral therapy and whether treatment was started before or after vaccination, age, vaccine strain, assays used to measure antibody concentrations, antibody levels considered protective, and exposure to wild-type pathogens that could confound antibody measurements. The small samples gave little power for comparisons, but several variables seemed to be associated with persistence of seroprotection. For example, as in immunocompetent persons, certain vaccine antigens, such as rubella, tetanus, and hepatitis A, induce more sustained responses than others [58]. The viro-immunologic status and use of antiretroviral therapy at the time of immunization is also critically important in maintaining seroprotection. As illustrated for measles, persistence of antibody concentrations was improved in children vaccinated or re-vaccinated during HAART [30, 32], as compared with others [25, 26, 27, 28, 29, 31]. More generally, patients immunized during HAART show prolonged seroprotection for most vaccine antigens, as illustrated in a recent review [59]. Similarly, HIV load at the time of immunization is an important independent predictor of persistence of seroprotection, as illustrated for hepatitis A [21, 22], yellow fever [55], and pneumococcal vaccines [43]. On the other hand, whereas increasing the dose of antigen is an interesting strategy to improve responses in immunocompromised hosts [60], there was no clear trend in our meta-analysis indicating that this strategy would extend the duration of seroprotection among primary responders.

Finally, antibody response is only one component of the immune response to vaccines. For some antigens (ie, measles, varicella, and yellow fever), cell-mediated immunity is the critical determinant of protection, and excluding its quantification may lead to a mistaken conclusion that boosters are required for all vaccines. Indeed, loss of antibodies does not necessarily imply loss of clinical protection, and immune memory can persist, even in individuals with low antibody concentrations [61]. As recently emphasized in a recent review: “a large variety of immune cells and functions are involved in controlling infections and any assignment of one as the mechanistic immune functions that contribute to protection (mCoP) must recognize that others may be involved as supplements or co-correlates of protection” [62]. In this respect, cellular responses seem to play a crucial role in the protection conferred by certain vaccines, and our choice to exclude reports on cell-mediated immunity lead to a certain degree of imprecision in the evaluation of immune responses. Evaluation of cell-mediated immunity provides important data on the degree of protection at an individual level, but methods of measurement are not routinely available and correlates of protection need to be established.

The clinical implications of this work need to be further explored in large prospective cohorts. In the future, the evaluation of new vaccines that specifically target persons with impaired immunity (inactivated or subunit zoster vaccine or cytomegalovirus vaccine) should confront clinical effectiveness with precise evaluation of the both humoral and cellular responses, in an attempt to establish reliable correlates of protection in these populations.

Supplementary Data

Supplementary materials are available at Clinical Infectious Diseases online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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Contributions. S. K. designed the study, performed the literature search, the statistical analysis, and the interpretation of the data and drafted the manuscript. O. L. contributed to the design of the study, the interpretation of the data, and the drafting of the manuscript. C. T. contributed to the statistical analysis, the interpretation of the data, and the drafting of the manuscript.
manuscript. F. B. contributed to the interpretation of the data and the drafting of the manuscript. T. H. contributed to the interpretation of the data and the drafting of the manuscript. P. Y. B. designed the study, performed the statistical analysis, and contributed to the interpretation of the data and the drafting of the manuscript.

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References

15. Pessoa SA, Miyamoto M, Ono E, Gouvêa AFTP, de Moraes-Pinto M, Succi RCM. Persistence of vaccine immunity against hepatitis B virus and response to revaccination in vertically HIV-infected adolescents on HAART. Vaccine 2010; 28:1606–12.
30. Melvin AJ, Mohan KM. Response to immunization with measles, tetanus, and Haemophilus influenzae type b vaccines in children who have human immunodeficiency virus type 1 infection and are treated with highly active antiretroviral therapy. Pediatrics 2003; 111:e641–4.
33. Teijolom C, Gouandjika I, Béniguel L, et al. HIV-infected children living in Central Africa have low persistence of antibodies to vaccines