Vaccines Must Be Given in Order to Protect

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(See the articles by Gallagher et al. and Moss et al., on pages 339–46 and 347–55, respectively.)

Two articles in this issue of the Journal [1, 2] highlight the importance and challenges of protecting HIV-infected individuals from 2 vaccine-preventable diseases, measles and influenza.

Great strides have been made recently in reducing deaths from measles. Between 1999 and 2005, mortality from measles dropped by 60%, from 873,000 to 345,000 deaths per year [3]. Seventy-five percent of this reduction occurred in Africa [4, 5]. This success is a result of substantial increases in measles vaccination coverage both through routine health services and mass vaccination campaigns. These accelerated control activities have been implemented by local Ministries of Health with the technical and financial support of the Measles Initiative, a partnership of multilateral, bilateral, and nongovernmental organizations spearheaded by 5 core members (the American Red Cross, the US Centers for Disease Control and Prevention, the United Nations Foundation, UNICEF, and the World Health Organization [WHO]) [5]. The strategy for achieving rapid reduction in measles mortality has 4 components: (1) improving routine immunization coverage to >90% in every district, (2) providing a second opportunity for measles immunization, (3) implementing effective measles surveillance, and (4) improving case management (e.g., with vitamin A and antibiotics).

That said, globally, measles remains one of the leading causes of deaths from a vaccine-preventable disease. In sub-Saharan Africa in 2005, there were still an estimated 126,000 measles-related deaths [3]. Often cited as a potential obstacle to achieving sustainable measles control is the HIV pandemic [6, 7]. In 2006, an estimated 2.1 million deaths from HIV occurred in this region [8].

Measles in children with HIV infection is more severe, resulting in a higher mortality. Infants born to HIV-infected mothers are at higher risk of measles at <9 months of age. Response to measles vaccination by HIV-infected children has been variable. In particular, limited data suggest that they have a lower response when vaccinated older than 12 months of age, presumably from increasing immune suppression [9–11]. Both the US Advisory Committee on Immunization Practices and the WHO recommend measles vaccination of HIV-infected children who are asymptomatic or have mild immunosuppression, regardless of antiretroviral therapy, although this is contraindicated in children with severe immunosuppression/AIDS [12, 13]. The WHO recommends that, given their high risk of measles at <9 months of age, HIV-infected infants (unless severely immunocompromised) should be vaccinated at 6 months of age with a second dose given at 9 months of age [13]. However, there are limited prospective studies evaluating the response to and optimal age of measles vaccination in HIV-infected children. In addition, most mothers are unaware of their children’s HIV status, making this recommendation more challenging to implement. Therefore, HIV-infected children are routinely vaccinated at 9 months of age, the same age as HIV-uninfected children.

These considerations make the study of Moss et al. [1], a prospective evaluation of the response of HIV-infected and -uninfected children to measles vaccination at 9 months of age, important. Their study demonstrates that HIV-infected children in Zambia showed a good primary response to measles vaccine but had rapidly waning antibodies over time. Their study also reiterated the high mortality in HIV-infected children in sub-Saharan Africa; of the 66 children who were HIV-infected at 9 months of age, 28 (42%) of them had died by 27 months of age. This high mortality not only makes it challenging to conduct prospective studies in this population but also may explain, in part, why countries in southern Africa have successfully controlled measles despite having high rates of HIV infection [14].
Although the study of Moss et al. showed a good response to revaccination against measles among HIV-infected children, other studies of children not receiving highly active antiretroviral therapy (HAART) have shown a less robust response to repeated measles vaccination, as previously reviewed [9]. The reason for the improved response in the current study is unclear. It may be partly a result of the younger age at revaccination and the shorter time interval before testing; children in Moss et al.’s study were revaccinated when <27 months of age and were tested only once a median of <3 months after revaccination, compared with testing at a median of 23–81 months in earlier studies [9]. In addition, given that mortality in Africa is quite high once persons develop symptomatic AIDS [15], it is possible that those in the study cohort who survived long enough to be revaccinated were less immunosuppressed.

This study also supports previous data of an increased susceptibility of HIV-infected children to measles before 9 months of age [16], because 13% of the 75 HIV-infected children developed measles at <9 months of age, compared with 5% of 621 uninfected children. Given that the response to measles vaccination is suboptimal in children vaccinated before 9 months of age, regardless of HIV status, the best way to protect these children from measles is through herd immunity by ensuring high measles vaccine coverage in the population. Specifically, it is important to ensure timely measles vaccination for all children, reached through a combination of routine health services and supplementary activities as a life-saving public health intervention in sub-Saharan Africa. In addition to the challenges of protecting HIV-infected children, this study also reminds us that HIV may only be one of the challenges to achieving high population immunity. Although malnutrition was not associated with poor response to measles vaccination in studies done in the 1970s–1990s [17–20], in this study malnourished children had a reduced response to measles vaccination, independent of their HIV status. These findings deserve further consideration.

This study was conducted before antiretroviral therapy became more generally available in Zambia. Studies in the United States have suggested that HIV-infected children receiving HAART have an improved response to measles vaccination, compared with those not receiving HAART [21, 22], although waning immunity may still be a problem [23]. HAART has also improved survival of HIV-infected children in developed countries. These findings will need to be replicated for HIV-infected children receiving antiretroviral therapy in sub-Saharan Africa. In addition, it will be important to compare the response of HIV-infected children in Zambia to measles vaccination at 9 months of age with a parallel study conducted in Malawi that was designed to assess a 6- and 9-month schedule in HIV-infected infants [24].

The key to protecting HIV-infected individuals from measles in the United States is the extremely high population immunity from high coverage rates for 2 doses of measles vaccine. Unfortunately, the United States has not been as successful at protecting its HIV-infected population from influenza, as demonstrated in the article by Gallagher et al. [2]. Influenza still kills an estimated 36,000 persons in the United States each year [25], and many of these deaths may be preventable with vaccination. Although influenza vaccination rates have increased, Gallagher et al. report that, as of 2002, the rates were still well under the recommended rate of 60% in all at-risk groups, including HIV-infected persons. Particularly striking, although nearly 90% of HIV-infected patients in their study had 2 or more health care visits during the influenza season, coverage with influenza vaccine only reached 42% in 2002. The reasons why providers did not ensure influenza vaccination for many HIV-infected patients warrant further study. In addition, it will be interesting to determine whether the vaccination coverage rates have increased since 2002 with the increasing attention given to influenza vaccination in the setting of pandemic influenza preparedness in the last few years.

Both of these articles point to the need to reinforce the best strategies to protect HIV-infected persons from vaccine preventable diseases, both in the United States and globally, until the HIV pandemic is controlled. Although there are clearly differences in target age groups, vaccines, and vaccination schedules, the basic public health principle of maintaining high vaccination coverage to achieve individual and population protection applies equally to 2 of the most highly infectious diseases in humans—measles and influenza.

References

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