*Immunizations in HIV and Aging*

There is a large body of data that vaccine preventable illnesses occur with greater frequency and are more severe in HIV-infected patients than in age-matched control subjects. Thus, a number of vaccines are indicated in HIV-infected subjects.

Consensus is widespread for use of most vaccines in persons living with HIV (PLWH) – these recommendations are nicely summarized in a recent Infectious Diseases Society of America Guideline for Vaccination of the Immunocompromised Host [1]. PLWH should be immunized according to the CDC schedule for adults (Figure 1). Regular primary and booster dose schedules based on age for Td/Tdap, hepatitis A and B, inactivated polio, and human papilloma virus (HPV), as well as annual influenza immunization and combination pneumococcal vaccines are suggested in PLWH (Figure 2). Live-attenuated organism vaccines are generally contraindicated, though in patients with a CD4 count > 200/mm3 mumps, measles and rubella (MMR) and varicella vaccines are indicated in patients not previously immunized. Particular caution should be noted in using yellow fever vaccine for travelers with HIV infection, but immunization can be considered for those at high risk of acquiring the disease during...
travel if they have asymptomatic HIV and CD4 counts are > 200 mm³.

**Current vaccine efficacy and evidence for a change in vaccine responsiveness with advancing age in PLWH.**

In persons without HIV infection, vaccine responsiveness declines with age, but differs by the vaccine. For example, hepatitis B vaccine responses begin to decline around age 35-40, whereas zoster and pneumococcal polysaccharide vaccine (PPV) responses begin waning about age 70-75 years [3]. Do vaccine responses wane at an earlier age in HIV-infected subjects and should this influence the recommended adult immunization schedule? Although data are limited, there is some suggestion that HIV does accelerate and/or enhance age-related declines in vaccine response. Two studies examined PPV and pneumonia prevention in HIV patients using age as a variable. Teshale et al. [5] showed that age 45+ was associated with all cause pneumonia even after adjustment for vaccine status indicating advanced age was associated with poorer vaccine efficacy. However, Rodriguez-Barradas et al. [6] found no such association in the VACS cohort. PPV was protective when pneumonia was examined as an outcome in that study only in HIV-infected subjects (average age 49 years). Efficacy of influenza vaccination in HIV-infected subjects has been examined in a number of studies with response dependent on CD4 count (Figure 3).

There is surprisingly little data on zoster vaccine in HIV-infected subjects despite substantial data on varicella vaccine. An ongoing trial (ClinTrials.gov # NCT00851786) may address this deficiency.
The most extensive examination of age and vaccine response in well-treated HIV-infected subjects was published [4]. Comparing HIV-infected, HAART-treated subjects < 40 (mean 31 yrs) vs. those > 50 (mean 59 years), all subjects had an undetectable viral load for 2 years and CD4 counts > 400. All had been immunized with tetanus toxoid (TT) during childhood, but not since; each subject was given a single TT boost. Age > 50 (Fig. 4) was associated with greatly reduced humoral (serum IgG) and cellular (T cell interferon production) responses after TT immunization. Additional in vitro studies show anti-IL-10 improves responses in aged HIV-uninfected patients, but not HIV-infected aged suggesting the mechanism of vaccine non-response differs. Since TT is a recall response, and naïve responses are more severely affected by age, one would anticipate naïve responses would be similarly, or more severely, reduced.

New Recommendations for Pneumococcal Immunization for HIV-infected Patients

The CDC now recommends that all adults aged 19 and older with immunocompromising conditions, which includes HIV, should be immunized. For those PLWH who have not previously received any pneumococcal vaccine one dose of the 13-valent protein-conjugated pneumococcal vaccine (PCV13) should be followed by a dose of pneumococcal polysaccharide vaccine (PPSV23) at least 8 weeks later. If the patient has previously received at least one dose of PPSV23, they should receive a single dose of PCV13 no sooner than 1 year after the last PPSV23 dose. If patients require another PPSV23 dose, it should be administered no sooner than 8 weeks after PCV13 and 5 years after the last PPSV23 dose.

![Figure 3. Seroprotection rate after standard-dose inactivated influenza vaccine (IIV) in Healthy control subjects vs. PLWH stratified by CD4 count at the time of immunization (Reproduced from [7] with permission).](image-url)
Efficacy of High Dose Inactivated Influenza Vaccine (IIV)

A high-dose IIV is available for individuals ≥65 years of age; FDA approval was based on data showing increased immunogenicity of the high-dose vaccine in older adults. A large randomized trial over two flu seasons to examine clinical efficacy was presented at a recent meeting of the Advisory Committee on Immunization Practices (ACIP) (http://www.cdc.gov/vaccines/acip/meetings/downloads/slides-oct-2013/04-Fluzone-Greenberg.pdf). High-dose (60 ug of protein) IIV was compared to standard dose (15 ug protein) IIV for clinical efficacy and had a relative efficacy of 24% (95% CI 9.7%-36.5%) compared with standard dose IIV. There were 227 lab-confirmed cases among the 15,892 participants who got high dose IIV, for a rate of 1.43%, and 300 cases among the 15,911 who received the standard dose IIV, for a rate of 1.83%. This exceeded the FDA-mandated definition required for superiority (lower bound of the 95% confidence interval > 9.1%). No HIV infected patients were knowingly included in this study, but HIV testing was not performed. At this time, however, the ACIP has not stated a preference for high-dose vaccine over the standard dose vaccine in older adults.

In a small clinical trial of HIV-infected patients (n=190) randomized to receive high-dose vs. standard-dose IIV immune responses were superior in the high-dose group, similar to the results noted above for seniors [8]. At this time, however, there is no recommendation to use high-dose IIV in HIV subjects unless they meet the age criteria, over 65, noted in Figure 1.
References


