*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

Figure 2. Vaccines that might be indicated for adults based on medical and other indications[1]

VACCINE ▼ INDICATION ►	Pregnancy	Immuno-compromising conditions (excluding human immunodeficiency virus [HIV])[4,6,7,8,15]	HIV infection CD4+ T lymphocyte count[4,6,7,8,15]: < 200 cells/μL	HIV infection CD4+ T lymphocyte count[4,6,7,8,15]: ≥ 200 cells/μL	Men who have sex with men (MSM)	Kidney failure, end-stage renal disease, receipt of hemodialysis	Heart disease, chronic lung disease, chronic alcoholism	Asplenia (including elective splenectomy and persistent complement component deficiencies)[8,14]	Chronic liver disease	Diabetes	Healthcare personnel
Influenza[2,*]	1 dose IIV annually				1 dose IIV or LAIV annually	1 dose IIV annually					1 dose IIV or LAIV annually
Tetanus, diphtheria, pertussis (Td/Tdap)[3,*]	1 dose Tdap each pregnancy	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs									
Varicella[4,*]	Contraindicated		2 doses								
Human papillomavirus (HPV) Female[5,*]		3 doses through age 26 yrs				3 doses through age 26 yrs					
Human papillomavirus (HPV) Male[5,*]		3 doses through age 26 yrs				3 doses through age 21 yrs					
Zoster[6]	Contraindicated				1 dose						
Measles, mumps, rubella (MMR)[7,*]	Contraindicated		1 or 2 doses								
Pneumococcal 13-valent conjugate (PCV13)[8,*]		1 dose									
Pneumococcal polysaccharide (PPSV23)[9,10]	1 or 2 doses										
Meningococcal[11,*]	1 or more doses										
Hepatitis A[12,*]	2 doses										
Hepatitis B[13,*]	3 doses										
Haemophilus influenzae type b (Hib)[14,*]	post-HSCT recipients only	1 or 3 doses									

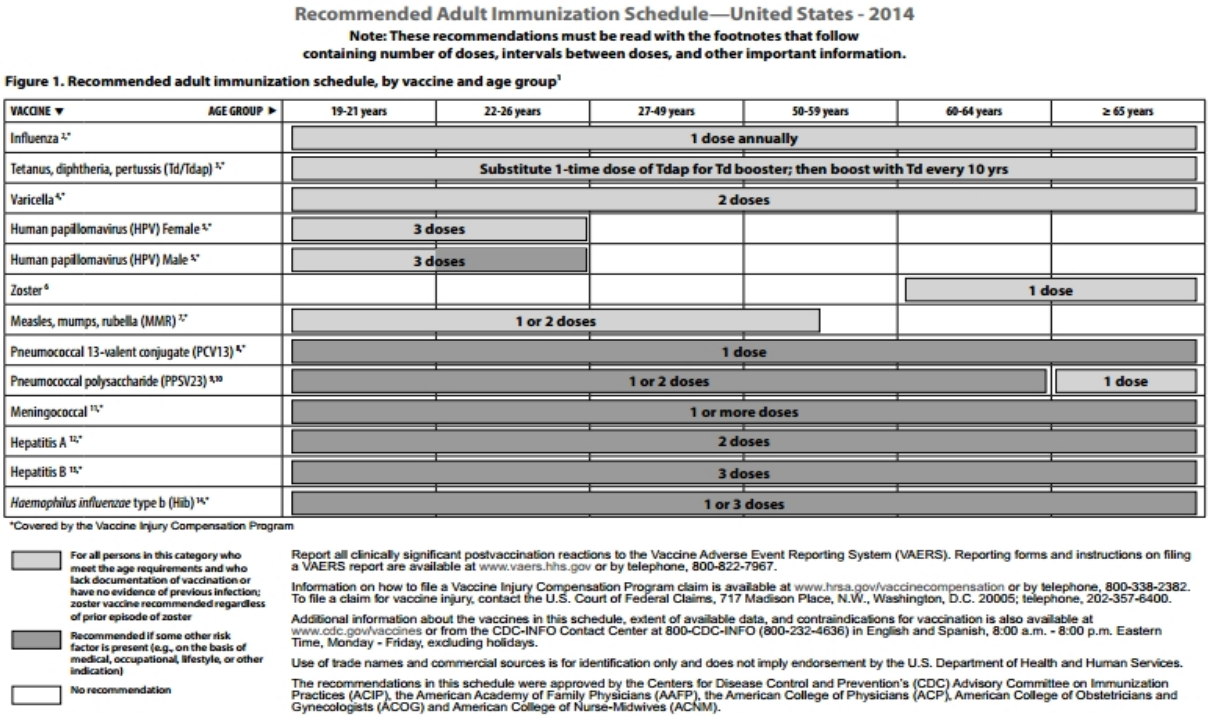
*Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indications)

No recommendation

Fig 2 Recommended vaccines based on immunocompromising condition including HIV. From CDC website http://www.cdc.gov/vaccines/schedules/downloads/adult/adult-schedule-bw.pdf



Recommended Adult Immunization Schedule—United States - 2014

Note: These recommendations must be read with the footnotes that follow containing number of doses, intervals between doses, and other important information.

Figure 1. Recommended adult immunization schedule, by vaccine and age group[1]

VACCINE ▼ / AGE GROUP ►	19-21 years	22-26 years	27-49 years	50-59 years	60-64 years	≥ 65 years
Influenza [2,*]	1 dose annually					
Tetanus, diphtheria, pertussis (Td/Tdap) [3,*]	Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 yrs					
Varicella [4,*]	2 doses					
Human papillomavirus (HPV) Female [5,*]	3 doses					
Human papillomavirus (HPV) Male [5,*]	3 doses					
Zoster [6]					1 dose	
Measles, mumps, rubella (MMR) [7,*]	1 or 2 doses					
Pneumococcal 13-valent conjugate (PCV13) [8,*]	1 dose					
Pneumococcal polysaccharide (PPSV23) [9,10]	1 or 2 doses					1 dose
Meningococcal [11,*]	1 or more doses					
Hepatitis A [12,*]	2 doses					
Hepatitis B [13,*]	3 doses					
Haemophilus influenzae type b (Hib) [14,*]	1 or 3 doses					

*Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack documentation of vaccination or have no evidence of previous infection; zoster vaccine recommended regardless of prior episode of zoster

Recommended if some other risk factor is present (e.g., on the basis of medical, occupational, lifestyle, or other indication)

No recommendation

Report all clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System (VAERS). Reporting forms and instructions on filing a VAERS report are available at www.vaers.hhs.gov or by telephone, 800-822-7967.

Information on how to file a Vaccine Injury Compensation Program claim is available at www.hrsa.gov/vaccinecompensation or by telephone, 800-338-2382. To file a claim for vaccine injury, contact the U.S. Court of Federal Claims, 717 Madison Place, N.W., Washington, D.C. 20005; telephone, 202-357-6400.

Additional information about the vaccines in this schedule, extent of available data, and contraindications for vaccination is also available at www.cdc.gov/vaccines or from the CDC-INFO Contact Center at 800-CDC-INFO (800-232-4636) in English and Spanish, 8:00 a.m. - 8:00 p.m. Eastern Time, Monday - Friday, excluding holidays.

Use of trade names and commercial sources is for identification only and does not imply endorsement by the U.S. Department of Health and Human Services.

The recommendations in this schedule were approved by the Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP), the American Academy of Family Physicians (AAFP), the American College of Physicians (ACP), American College of Obstetricians and Gynecologists (ACOG) and American College of Nurse-Midwives (ACNM).

Figure 1: Recommended vaccine schedule for adults based on age From CDC website http://www.cdc.gov/vaccines/schedules/downloads/adult/adult-schedule-bw.pdf .

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.

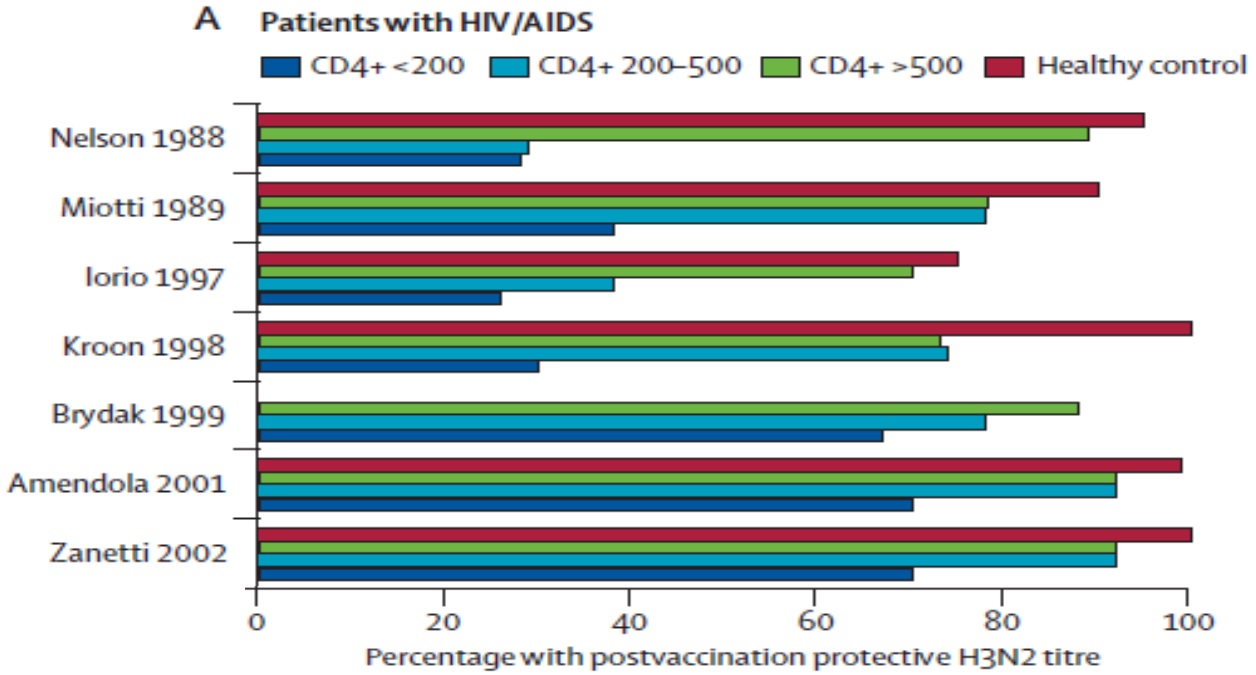


Figure 3. Seroprotection rate after standard-dose inactivated influenza vaccine (IIV) in Healthy control subjects vs. PLWH stratified by CD4 count at the time of immunization (Reproduced from [7] with permission).

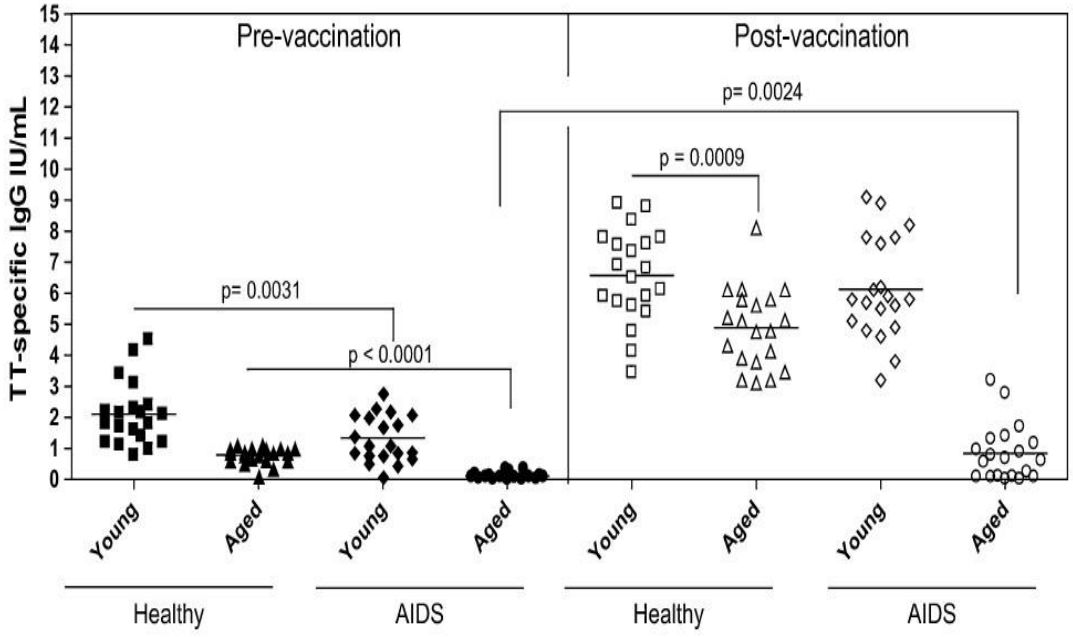


Figure 4. Failure of HAART to Reconstitute Immune Response to Tetanus Toxoid Vaccine in Aged AIDS Patients. From [4] Used by permission of the publisher.

(http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6140a4.htm).

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

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