AETC AIDS Education & Training Center Program Southeast

Immunization Essentials for Adults with HIV

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Disclosures

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- This slide set has been peer-reviewed to ensure that there are no conflicts of interest represented in the presentation

Objectives

- Describe the differences in immunization requirements for persons living with HIV
- Recommend appropriate vaccinations to adult and geriatric persons living with HIV
- Discuss current clinical controversies related to immunizations in persons living with HIV

Background- Importance of Vaccinations

- Persons living with HIV (PLWH) are at an increased risk of many different infections
- Higher risk and severity of pneumonia due to *Streptococcus pneumoniae* and influenza virus
- Higher risk of disease progression (cirrhosis, hepatocellular carcinoma) with hepatitis B
- Higher risk of rapid progression of human papillomavirus (HPV) related cancers

Chaturvedi AK et al. J Natl Cancer Inst. 2009;101:1120–30.

By The Numbers…

- Higher risk and severity of pneumonia due to *Streptococcus pneumoniae* and influenza virus[1]
  - Greater risk of IPD aRR of 6.6 (95% CI:2.7–16.1,p < 0.001) in 2010-11
- Higher risk of disease progression with Hepatitis B[2]
  - All cause mortality much higher in men with HIV than those without (RR 33.8 (95%CI 26.6-43.8, p<0.001)
- Higher risk of rapid progression of Human papillomavirus (HPV) related cancers[3]
  - Compared to general population (SIRs* ranged from 8.9, 95% CI = 8.0 to 9.9, for cervical cancer to 68.6, 95% CI = 59.7 to 78.4, for anal cancer among men)

*standardized incidence ratios (SIRs)

1. AIDS Patient Care STDS. 2016 Oct;30(10):463-470. 2.Thio CL et al. Lancet 2002;360:1921–6. 3.Chaturvedi AK, . J Natl Cancer Inst. 2009;101:1120–30.

Infectious Disease Risk Reduction Strategies in PLWH

- Receipt of antiretroviral therapy (ART) to enhance immune system
- Behavioral risk modifications
  - Smoking cessation (influenza and pneumonia)
  - Safe sex (HBV and HPV)
- Prophylaxis (based on CD4 cell count)
- **Vaccination**

Important Considerations

- Vaccination is a key component to ensure the health of all persons living with HIV
- People who are born in other countries may have had incomplete childhood vaccinations
- Catch up vaccination for some childhood vaccines depending on risks, including MMR/Varicella if CD4 count > 200 cells/mL

Figure 2. Recommended immunization schedule for adults aged 19 years or older by medical condition and other indications, United States, 2018

This figure should be reviewed with the accompanying footnotes. This figure and the footnotes describe indications for which vaccines, if not previously administered, should be administered unless noted otherwise.

Vaccine	Pregnancy[1-6]	Immuno-compromised (excluding HIV infection)[3-7,11]	HIV infection CD4+ count (cells/μL)[3-7,9-10]		Asplenia, complement deficiencies[7,10,11]	End-stage renal disease, on hemodialysis[7,9]	Heart or lung disease, alcoholism[7]	Chronic liver disease[7-9]	Diabetes[7,9]	Health care personnel[3,4,9]	Men who have sex with men[6,8,9]
			<200	≥200							
Influenza[1]	1 dose annually										
Tdap[2] or Td[2]	1 dose Tdap each pregnancy	1 dose Tdap, then Td booster every 10 yrs									
MMR[3]	contraindicated			1 or 2 doses depending on indication							
VAR[4]	contraindicated			2 doses							
RZV[5] (preferred)					2 doses RZV at age ≥50 yrs (preferred)						
or					or						
ZVL[5]	contraindicated				1 dose ZVL at age ≥60 yrs						
HPV–Female[6]		3 doses through age 26 yrs			2 or 3 doses through age 26 yrs						
HPV–Male[6]		3 doses through age 26 yrs			2 or 3 doses through age 21 yrs						2 or 3 doses through age 26 yrs
PCV13[7]		1 dose									
PPSV23[7]		1, 2, or 3 doses depending on indication									
HepA[8]	2 or 3 doses depending on vaccine										
HepB[9]	3 doses										
MenACWY[10]	1 or 2 doses depending on indication , then booster every 5 yrs if risk remains										
MenB[10]	2 or 3 doses depending on vaccine										
Hib[11]	3 doses HSCT recipients only	1 dose									

Recommended for adults who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended for adults with other indications

Contraindicated

No recommendation

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Immunizations Recommended For General Population

Influenza vaccine

- Annual inactivated influenza vaccine

Tetanus-diphtheria (Td)/tetanus-diphtheria-pertussis (Tdap)

- Tdap once, Td every 10 years

Human papillomavirus (HPV) vaccine

- 3 dose vaccination series*

* For those aged < 26 years

Kim DK et al. MMWR Morb Mortal Wkly Rep. 2018 Feb 9;67(5):158-160.

Additional Immunization Considerations for Persons Living with HIV

Pneumococcal vaccines

- 13-valent pneumococcal conjugate vaccine (PCV13), followed by 23-valent pneumococcal polysaccharide vaccine (PPSV23)*

Meningococcal vaccine

- MenACWY (serogroups A, C, W, and Y) 2 doses, booster every 5 years

Hepatitis B vaccine

- 3 or 4 dose series

Hepatitis A vaccine (for most PLWH)

- 2 or 3 dose series (depending on vaccine)

*additional doses, depending on if age > 65 yrs

Kim DK et al. MMWR Morb Mortal Wkly Rep. 2018 Feb 9;67(5):158-160.

Pneumococcal Vaccines Two Types

13-valent pneumococcal conjugate vaccine (PCV13)	23-valent pneumococcal polysaccharide vaccine (PPSV23)
• T-cell–dependent immune response • T cells provide the signals needed for maturation of the B-cell response and generation of B-cell memory	• T-cell independent immune response (limited to 3–5 yrs)

PCV + PPSV?

Immunological efficacy of pneumococcal vaccine strategies in HIV-infected adults: a randomized clinical trial

C. Sadlier[1,2], S. O'Dea[1], K. Bennett[3], J. Dunne[4], N. Conlon[4] & C. Bergin[1,2]

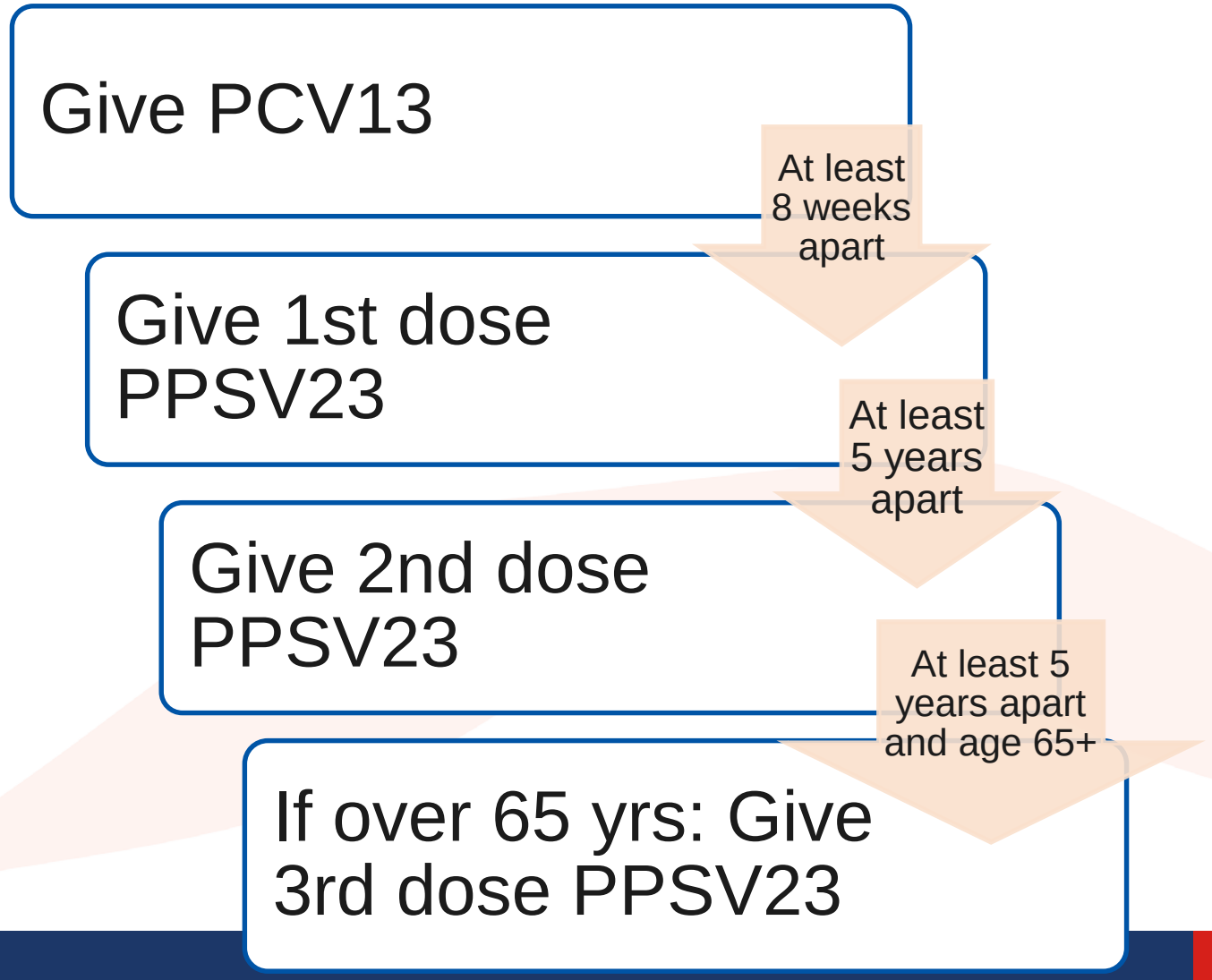
- The aim: to compare the immunologic response prime-boost immunization strategy vs. standard
  - PCV13 with PPSV23 vs. PPSV23 alone in HIV-infected adults
- N= 31 in combo N= 33 in PPSV23 alone
- Proportion of 4-fold serotype OPA* responses was significantly greater in the prime-boost group vs. the PPSV23-alone group
  - Week 8 OR 1.71, 95%CI 1.22–2.39
  - Week 28 OR 1.6, 95% CI 1.15–2.3

*functional oposonophagocytic (OPA) geometric mean titer (GMT)

Sadlier, C. et al. Immunological efficacy of pneumococcal vaccine strategies in HIV infected adults: a randomized clinical trial. Sci. Rep. 6, 32076; doi: 10.1038/srep32076 (2016).

Recommended Schedule

- 13-valent pneumococcal conjugate vaccine (PCV13) followed by a 23-valent pneumococcal polysaccharide vaccine (PPSV23)



Kim DK et al. MMWR Morb Mortal Wkly Rep. 2018 Feb 9;67(5):158-160.

Hepatitis B Vaccination

- PLWH should be screened for evidence of hepatitis B virus (HBV) infection upon initiation of care
  - Hepatitis B surface antigen (HBsAg)
  - Hepatitis B surface antibody (HBsAb)
  - Antibody to hepatitis B total core antigen (anti-HBc or HBcAb)
- Susceptible patients should be vaccinated

(*strong recommendation, high quality evidence*)

Aberg JA et al. Clin Infect Dis. 2014;58:e1–34

Hepatitis B Vaccination

- Current ACIP recommendations state:

> "Modified dosing regimens, including a doubling of the standard antigen dose or administration of additional doses, might increase response rates. However, data on response to these alternative vaccination schedules are limited"

- Three options:
  - Standard dose 3 series vaccination
  - Double dose 3 or 4 series vaccination
  - *New adjuvanted vaccine 2 dose series?*

Schillie S. et al. MMWR Recomm Rep 2018;67(1-36)

Available Hepatitis B Vaccines

Engerix-B

- Has a 1 mL 20 mcg dose available
- Standard schedule: 3-doses at 0, 1, and 6 months
- Double dose: Two 1 mL doses administered at one site, on a 4-dose schedule at 0, 1, 2, and 6 months [2]

Recombivax HB

- Has a 1 mL 40 mcg dose available (dialysis formulation)
- 3-dose schedule at 0, 1, and 6 months

Heplisav-B [Adjuvanted with Cytosine phosphoguanine (CpG) 1018]*

- *Administer two doses (0.5 mL each) one month apart*
- *Recently FDA approved 11/2017*

*data with HIV is lacking

1. Kim DK et al. MMWR Morb Mortal Wkly Rep. 2018 Feb 9;67(5):158-160.
2. Aberg JA et al. Clin Infect Dis. 2014;58:e1–34

Hepatitis A Vaccination Indications

- men who have sex with men
- injection drug users
- travelers to countries of high endemicity
- persons with chronic liver disease
- persons infected with hepatitis B and/or C

Kim DK et al. MMWR Morb Mortal Wkly Rep. 2018 Feb 9;67(5):158-160.

Available Hepatitis A Vaccines

Havrix (Hepatitis A Vaccine)

- 2 doses, 1 mL, first followed by booster in 6-12 months

Vaqta (Hepatitis A Vaccine)

- 2 doses, 1 mL, first followed by booster in 6-8 months

Twinrix [Hepatitis A & Hepatitis B (Recombinant) Vaccine]

- 3 doses, 1 mL, followed by doses at 1 and 6 months
- Contains 20 mcg of Hepatitis B antigen
- Accelerated dosing: A series of 4 doses given on days 0, 7, and 21 to 30 followed by a booster dose at month 12

Human papillomavirus (HPV)

Indicated for all PLWH under 26 years of age

Quadrivalent vaccine Gardasil-4

- *Four serotypes (HPV 6, 11, 16, and 18)*
- *3-dose series at 0, 1–2, and 6 months*
- No longer available

Nine-valent vaccine Gardasil-9

- Nine serotypes (HPV 6, 11, 16, 18, 31, 33, 45, 52, and 58)
- Covers an additional 14% of female cancers and 4% of male cancers
- **3-dose series** at 0, 1–2, and 6 months

*Although some patients can do a 2-dose series depending on age of vaccine initiation, this is not recommended for PLWH

Kim DK et al. MMWR Morb Mortal Wkly Rep. 2018 Feb 9;67(5):158-160.

Influenza Vaccination

- Live attenuated influenza vaccine (LAIV) was not recommended for the 2017–2018 influenza season, and it is contraindicated in PLWH

- ACIP recommendation: Inactivated influenza vaccine (IIV) or recombinant influenza vaccine (RIV) annually

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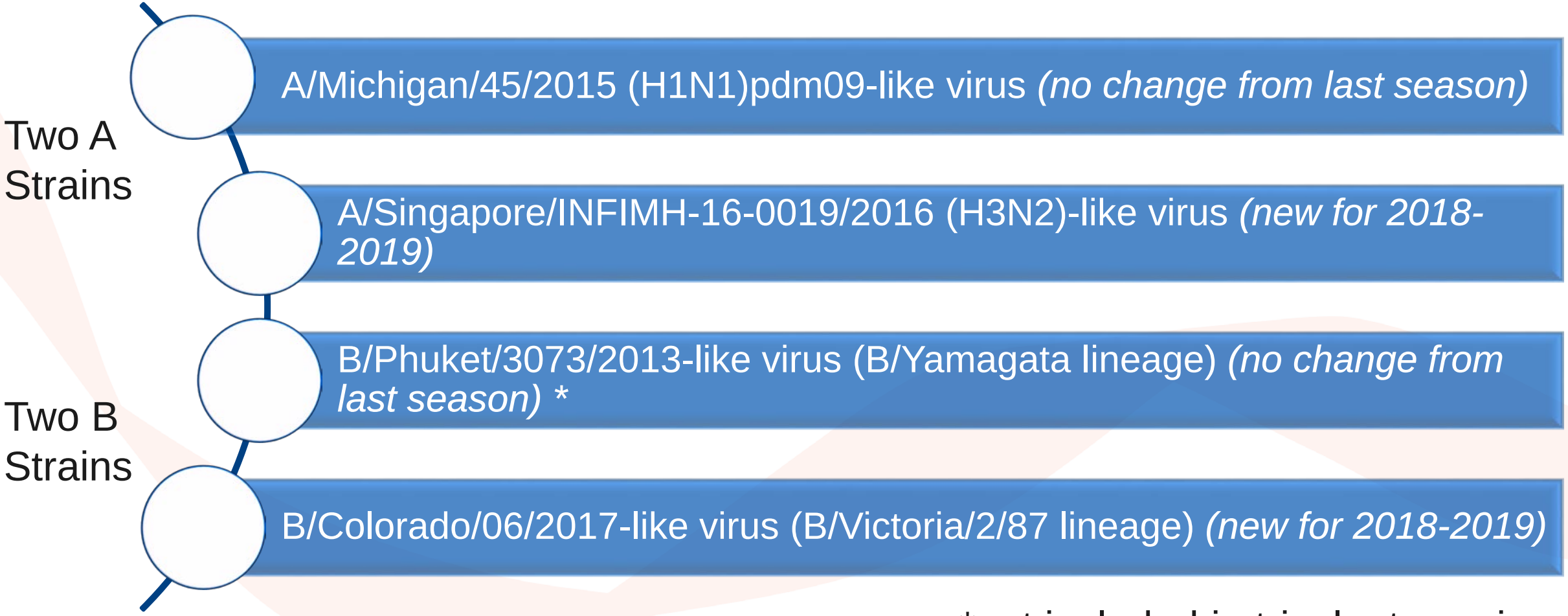
Vaccine Strains For 2018-2019



*not included in trivalent vaccines

Influenza Vaccines 2017-2018 season

- Inactivated influenza vaccines, quadrivalent (IIV4s) or trivalent (IIV3s) standard-dose
  - 15 *µ*g of each vaccine HA antigen
- Adjuvanted inactivated influenza vaccine, trivalent (aIIV3), standard-dose
- Inactivated influenza vaccine, quadrivalent (ccIIV4), standard-dose, cell culture-based
- Inactivated influenza vaccine, trivalent (IIV3), high-dose
  - 60 *µ*g of each vaccine antigen
  - Approved for adults over 65 years
- Recombinant influenza vaccine, quadrivalent (RIV4) or trivalent (RIV3)

Tetanus-diphtheria-pertussis vaccination

- **Tdap** Tetanus-diphtheria-pertussis
  - One time dose recommended for all adults
    - Additional doses may be indicated if caring for infants or pregnant
  - Adacel
  - Boostrix
- **Td** Tetanus-diphtheria
  - Booster every 10 years
  - Tenivac
  - Td generic

Kim DK et al. MMWR Morb Mortal Wkly Rep. 2018 Feb 9;67(5):158-160.

Meningococcal Vaccines

MenACWY (serogroups A, C, W, and Y meningococcal vaccine)	Serogroup B meningococcal vaccine (MenB)
• Conjugate vaccine (Menactra) • Conjugate vaccine (Menveo) • 2 doses at least 8 weeks apart • Booster every 5 years	• MenB-4C (Bexsero) • MenB-FHbp (Trumenba) • *Optional: ages 16–23 years* • Both 2 doses, Not interchangeable

MPSV4 (4-valent meningococcal polysaccharide vaccine) is no longer available and has been removed from the adult immunization schedule.

Kim DK et al. MMWR Morb Mortal Wkly Rep. 2018 Feb 9;67(5):158-160.

Childhood Vaccines if CD4 > 200 cells/mL*

MMR vaccine

- To protect against measles, mumps, and rubella
- If born in 1957 or after and have not gotten this vaccine or do not have immunity to these diseases

Varicella vaccine

- To protect against chickenpox
- If born in 1980 or after and have not gotten two doses of this vaccine or do not have immunity to this disease

*CD4 percentage should be 15% or greater.

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Patient Case Question

- Mr. Y is a 38 year old MSM, born in the U.S. who was recently diagnosed with HIV and started on ART immediately. His current viral load is < 20 copies/mL and CD4 count is 300 cells/mL. His baseline labs include HepB serologies which show immunity. He is here at the clinic for immunizations as he has not received any vaccines since childhood.
- Which of the following is an appropriate vaccine recommendation for today?

A. PPSV23, Hepatitis A and HPV
B. PCV13, Hepatitis A, and Td
C. PCV13, Hepatitis A, MenACWY, Tdap
D. PCV13, MenACWY and Tdap

Patient Case Question

- Ms. L is a 24 year old heterosexual female, born in the U.S. who was recently diagnosed with HIV and started on ART immediately. She is currently undetectable and CD4 count is 450 cells/mL. She was previously up-to-date with all childhood vaccines up until age 20. She is here at the clinic for any additional immunizations she would need due to her HIV diagnosis.
- Which of the following is the most appropriate option at this visit (in June)?

A. HepB, MenACWY, and PCV13
B. Serology for HepB immunity, MenACWY, and PCV13
C. Serology for HepB immunity, MenACWY, Inactivated Influenza Quadrivalent and PCV13
D. HepB, PPSV23 and PCV13

Patient Case Question

- Ms. L is a 24 year old heterosexual female, born in the U.S. who was recently diagnosed with HIV and started on ART immediately. She is currently undetectable and CD4 count is 450 cells/mL. She was previously up-to-date with all childhood vaccines up until age 20.
- Which of the following is true regarding her pneumococcal vaccination recommendations?

A. PPSV23 now and PCV13 in 6 months
B. PCV13 now and PPSV23 in 1 year
C. PCV13 now and PPSV23 at next visit (3 months)
D. PPSV23 now and PCV13 at next visit (3 months)

CLINICAL CONTROVERSIES RELATED TO IMMUNIZATIONS IN PERSONS LIVING WITH HIV

Shingles Vaccine?

- ACIP has no recommendations related to the new herpes zoster vaccine available for its use in PLWH
- In the general population:
  - Adults aged 50 years+ should receive a 2 doses series of recombinant zoster vaccine (RZV) (Shingrix) 2–6 months apart
  - The RZV is preferred in general population > ZVL (live zoster)

- Previously, the only vaccine available was a live vaccine
  - This is contraindicated in patients with CD4 < 200 cells/mL.

Kim DK et al. MMWR Morb Mortal Wkly Rep. 2018 Feb 9;67(5):158-160.

Hepatitis B Vaccine Dosing

- The humoral response to HepB vaccine is reduced in children and adults who are immunocompromised
- Modified dosing regimens, including a doubling of the standard antigen dose or administration of additional doses, might increase response rates.
  - However, data on response to these alternative vaccination schedules are limited

Kim DK et al. MMWR Morb Mortal Wkly Rep. 2018 Feb 9;67(5):158-160.

Hepatitis B Vaccine Dosing

- Meta-analysis including 5 clinical studies (n = 883 PLWH, mostly vaccine naive) HD vs SD
- HD double dose (40 mcg/ml)
- SD standard dosing (20 mcg) *9% of SD got 10 mcg
- N= 883
- Significant increase in response rates using the higher dose vaccine (OR 1.96, 95% CI 1.47–2.61)

Ni JD et al. Int J STD AIDS. 2013;24:117–22.

Influenza Vaccine Efficacy

- The efficacy of influenza vaccination among HIV-infected persons is reduced compared with HIV-uninfected persons[1]
- Strategies to improve efficacy
  - Higher dose (4x amount of antigen)? [2]
  - Optimize timing?[3,4]
  - Studies are small, recommendations are the same as general population

1. Infect Dis Ther. 2017 Sep;6(3):303-331 2. McKittrick N. et al. Ann Intern Med. 2013;158:19–26.
3. Ferdinands JM et al. Clin Infect Dis. 2017;64:544–50 4. Crum-Cianflone NF et al. Vaccine. 2011;29:3183–91.

Influenza Vaccine Dosage

- Single-site, double-blind, RCT comparing the immunogenicity of a highdose (HD) influenza vaccine with the standard dose (SD) in PLWH
- Primary outcome seroprotective antibody levels at 21-28d
- Seroconversion rates were greater in the HD group than in the SD group
  - H1N1 (75% vs. 59%) **p=0.018**
  - H3N2 (78% vs. 74%) p =0.5
  - influenza B (56% vs. 34%) **p=0.003**

McKittrick N. et al. Ann Intern Med. 2013;158:19–26.

Influenza Vaccine Timing

- Evaluation of immunogenicity of a monovalent 2009 influenza A (H1N1) vaccine
- Primary objective: compare seroconversion rates among HIV-infected and HIV-uninfected adults at day 28
- HIV-infected compared to HIV-uninfected adults were less likely to generate a seroprotective response at day 28 or a durable response at 6 months post-vaccination

Outcome Seroconversion	HIV+ N (%)	HIV – N (%)	Adjusted OR (95% CI)	P-value
Day 28:titer ≥1:40	25/46 (54%)	27/36 (75%)	0.23 (0.06, 0.76)	p=0.021
Month 6:titer ≥1:40	13/46 (28%)	20/36 (56%)	0.19 (0.06, 0.59)	p=0.005

Crum-Cianflone NF et al. Vaccine. 2011;29:3183–91.

Influenza Vaccine Timing

- The US Influenza Vaccine Effectiveness Network Study
- Patients who had illness with cough and/or fever/feverishness were tested with NP PCR
- Adjusted vaccine effectiveness (VE) decreased with time.

Influenza A(H3N2)	Maximum VE of 35% at 14 days postvaccination, and VE reaching zero at **158 days postvaccination**
Influenza A(H1N1)pdm09	Maximum VE of 80% at 14 days postvaccination and minimum VE of 37% at **128 days postvaccination**
Influenza B	Maximum VE of 59% at 14 days postvaccination and minimum VE of 23% at **180 days postvaccination**

Ferdinands JM et al. Clin Infect Dis. 2017;64:544–50.

Other Key Things to Remember

- Always give a Vaccine Information Sheet (VIS)
- Documentation and updating state vaccine record (if available)
- Patients born outside of the U.S may need to be evaluated for risk and catch up vaccines

References

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Questions?

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