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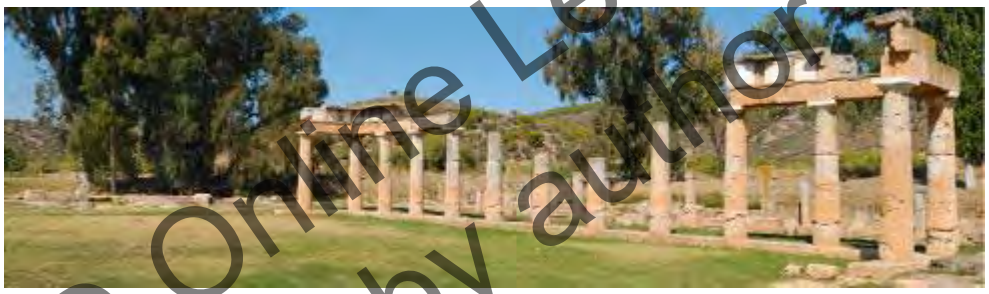

Primary prevention of opportunistic infections in HIV-infected patients.

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Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents

Recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America

Prophylaxis

- Frequency of OI
- Survival benefits associated with prophylaxis
- Drug interactions
- Potential drug resistance
- Cost

Pneumocystis Pneumonia

- *Pneumocystis* pneumonia (PCP) is caused by *Pneumocystis jirovecii*, a ubiquitous organism that is classified as a fungus.
- Approximately 90% of cases occurred among patients with CD4+ counts of <200 cells/*μL*.

Pneumocystis Pneumonia

- Before the widespread use of primary PCP prophylaxis and ART
  - PCP occurred in 70%–80% of patients with AIDS
  - mortality *of 20%–40%*

Preventing Exposure

- Certain authorities might recommend that persons who are at risk for PCP not share a hospital room with a patient who has PCP
- A recommendation based on animal studies and anecdotal human experience.
- Data are insufficient to support this recommendation as standard practice (CIII).

Prophylaxis to prevent first episode of opportunistic disease - When

- CD4+ count <200 cells/μL (AI) or oropharyngeal candidiasis (AII)
- CD4+ <14% or history of AIDS-defining illness (BII)
- CD4+ count >200 but <250 cells/μL
  - if monitoring CD4+ every 1–3 months not possible

Prophylaxis to prevent first episode of opportunistic disease - What

- Trimethoprim-sulfamethoxazole (TMP-SMX)
  - 1 DS PO daily (AI)
  - 1 SS daily (AI)
    - one single-strength tablet daily also is effective and might be better tolerated than one double-strength tablet daily

Prophylaxis to prevent first episode of opportunistic disease - Alternatives

- TMP-SMX 1 DS PO tiw (BI);
- Dapsone 100 mg PO daily or 50 mg PO bid (BI);
- Dapsone 50 mg PO daily + pyrimethamine 50 mg PO weekly + leucovorin 25 mg PO weekly (BI);
- Aerosolized pentamidine 300 mg every month (BI)
- Atovaquone 1,500 mg PO daily (BI);

Toxoplasmic encephalitis

- Toxoplasmic encephalitis (TE) is caused by the protozoan *Toxoplasma gondii.*
- *Disease appears to occur almost exclusively because of reactivation of latent tissue cysts*
- *The greatest risk occurs among patients with a CD4+ count <50 cells/μL*

Toxoplasmic encephalitis

- Seroprevalence
  - 15% in the United States
  - 50%–75% in certain European countries
- In patients who are seropositive for *T. gondii*
  - *the 12-month incidence of TE is approximately 33%.*

Preventing Exposure

- HIV-infected persons should be tested for IgG antibody to *Toxoplasma* soon after the diagnosis of HIV infection to detect latent infection with *T. gondii* (BIII).
- HIV-infected persons should be advised not to eat raw or undercooked meat, including undercooked lamb, beef, pork, or venison (BIII).
- HIV-infected persons should wash their hands after contact with raw meat and after gardening or other contact with soil;
- They should wash fruits and vegetables well before eating them raw (BIII).

If the patient owns a cat Kill the cat?

- *The litter box should be changed daily, preferably by an HIV-negative, nonpregnant person; alternatively, patients should wash their hands thoroughly after changing the litter box (BIII).*
- *Patients should be encouraged to keep their cats inside and not to adopt or handle stray cats (BIII).*
- *Cats should be fed only canned or dried commercial food or well-cooked table food, not raw or undercooked meats (BIII).*
- *Patients need not be advised to part with their cats or to have their cats tested for toxoplasmosis (EII).*

Prophylaxis to prevent first episode of opportunistic disease - When

- Toxoplasma IgG positive patients with CD4+ count <100 cells/μL (AII)
- Seronegative patients should have toxoplasma serology retested if CD4+ count decline to <100 cells/μL (CIII)
- Prophylaxis should be initiated if seroconversion occurred (AII)

Prophylaxis to prevent first episode of opportunistic disease - What

- TMP-SMX, 1 DS PO daily (AII)

Prophylaxis to prevent first episode of opportunistic disease - Alternatives

- TMP-SMX 1 DS PO tiw (BIII);
- TMP-SMX 1 SS PO daily (BIII);
- Dapsone 50 mg PO daily +pyrimethamine 50 mg PO weekly +leucovorin 25 mg PO weekly (BI);
- (Dapsone 200 mg + pyrimethamine 75 mg + leucovorin 25 mg) PO weekly (BI);
- (Atovaquone 1,500 mg +/- pyrimethamine 25 mg + leucovorin 10 mg) PO daily (CIII)

Tuberculosis

- The World Health Organization (WHO) estimates that TB is the cause of death for 13% of persons with AIDS
- CD4+ count is not a reliable predictor of increased risk for TB disease in HIV-infected persons.

HIV-infected persons at increased risk for acquiring TB

- Live or work in high-risk settings
  - correctional facilities,
  - health-care facilities,
  - homeless shelters

Tuberculosis

- TB infection occurs when a susceptible person inhales droplet nuclei containing *Mycobacterium tuberculosis* organisms
- Usually within 2–12 weeks after infection, the immune response limits multiplication of tubercle bacilli.
- However, viable bacilli persist for years, a condition referred to as latent TB infection (LTBI).

Tuberculosis

- TB disease can develop
  - immediately after exposure (primary disease) or
  - after reactivation of LTBI (reactivation disease).
- Primary disease accounts for one third or more of cases of TB disease in HIV-infected populations
- rates of progression to active TB among HIV-infected persons with LTBI is 3-10 times higher than among HIV-negative patients

Tuberculosis

- All persons should be tested for LTBI at the time of HIV diagnosis regardless of their TB risk category **(AII).**
- should be re-tested for LTBI once they start ART and attain a CD4+ count >200 cells/*µL* ***(AIII)***
- annual testing for LTBI is recommended for HIV-infected persons who are or remain in a "high-risk"

Tuberculosis

- All HIV-infected persons with a positive diagnostic test for LTBI should undergo chest radiography and clinical evaluation to rule out active TB **(AI).**

Diagnosis

- The tuberculin skin test (TST), is considered positive in HIV-infected persons if induration of >5 mm
- Evidence suggests that the IGRAs have more consistent and higher specificity (92%–97%) compared with TST (56%–95%).

Prophylaxis to prevent first episode of opportunistic disease - When

- (+) diagnostic test for LTBI, no evidence of active TB, and no prior history of treatment for active or latent TB (AI);
- (-) diagnostic test for LTBI, but close contact with a person with infectious pulmonary TB and no evidence of active TB (AII);
- A history of untreated or inadequately treated healed TB (i.e., old fibrotic lesions) regardless of diagnostic tests for LTBI and no evidence of active TB (AII)

Prophylaxis to prevent first episode of opportunistic disease - What

- Isoniazid (INH)
  - 300 mg PO daily (AII) or
  - 900 mg PO biw (BII)
- for 9 months – both plus pyridoxine 50 mg PO daily (BIII);
- Alternatives
  - Rifampin (RIF) 600 mg PO daily x 4 months (BIII); or
  - • Rifabutin (RFB) (dose adjusted based on concomitant ART) x 4 months (BIII)

Disseminated *Mycobacterium avium Complex* Disease

- Organisms of the *Mycobacterium avium complex (MAC)* are ubiquitous in the environment
- *M. avium* is the etiologic agent in >95% of patients with AIDS who acquire disseminated MAC disease
- incidence is 20%–40%
- MAC disease typically occurs among persons with CD4+ counts <50 cells/*μL.*

Disseminated *Mycobacterium avium* Complex Disease

- Other factors for MAC disease
  - high plasma HIV RNA levels (>100,000 copies/mL),
  - previous OIs,
  - previous colonization of the respiratory or gastrointestinal tract with MAC,

Disseminated *Mycobacterium avium* Complex Disease

- MAC disease is typically a disseminated multi-organ infection.
- Symptoms include
  - fever,
  - night sweats,
  - weight loss,
  - fatigue,
  - diarrhea,
  - abdominal pain

Disseminated *Mycobacterium avium* Complex Disease

- Localized syndromes include
  - cervical or mesenteric lymphadenitis,
  - pneumonitis,
  - pericarditis,
  - osteomyelitis,
  - skin or soft tissue abscesses,
  - genital ulcers,
  - CNS infection.

Prophylaxis to prevent first episode of opportunistic disease - When

- CD4+ count <50 cells/µL – after ruling out active MAC infection (AI)

Prophylaxis to prevent first episode of opportunistic disease - What

- Azithromycin 1,200 mg PO once weekly (AI);
- Clarithromycin 500 mg PO bid (AI);
- Azithromycin 600 mg PO twice weekly (BIII)
- Alternative
  - RFB 300 mg PO daily (BI) (dosage adjustment based on drug-drug interactions with ART);

Bacterial pneumonia

- Bacterial pneumonia is a common cause of HIV-associated morbidity
- incidence 3.9–7.3 episodes per 100 person-years
- *Streptococcus pneumoniae* and *Haemophilus species*
- *S.pneumoniae* pneumonia
  - increased incidence of bacteremia

Streptococcus pneumoniae infection - vaccine

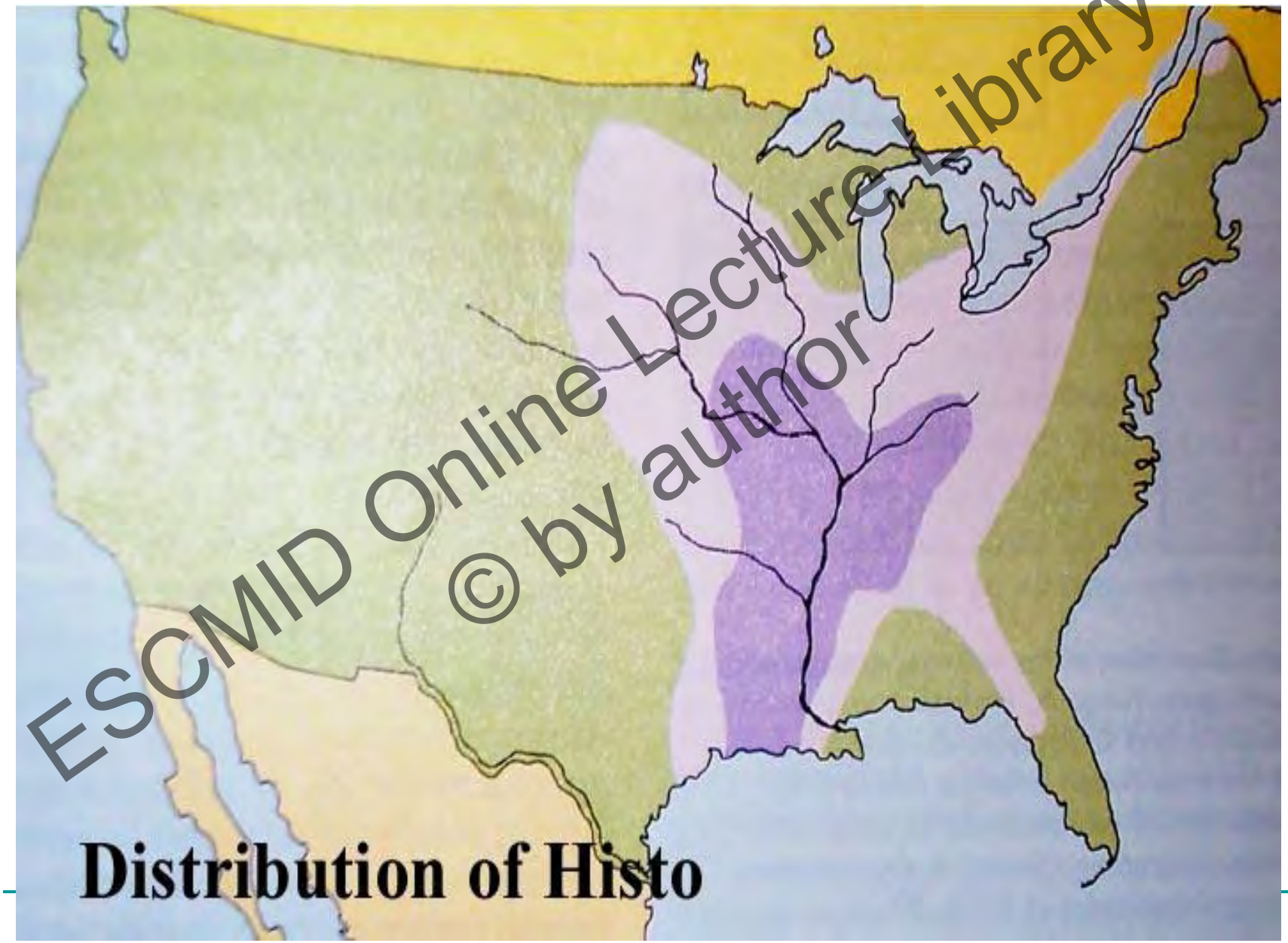
- CD4+ count >200 cells/μL and no receipt of pneumococcal vaccine in the past 5 years (AII)
- CD4+ count <200 cells/μL – vaccination can be offered (CIII)
- polysaccharide pneumococcal vaccination (PPV),

Influenza A and B virus infection

- All HIV-infected patients (AIII)
- Inactivated influenza vaccine 0.5 mL IM annually (AIII)

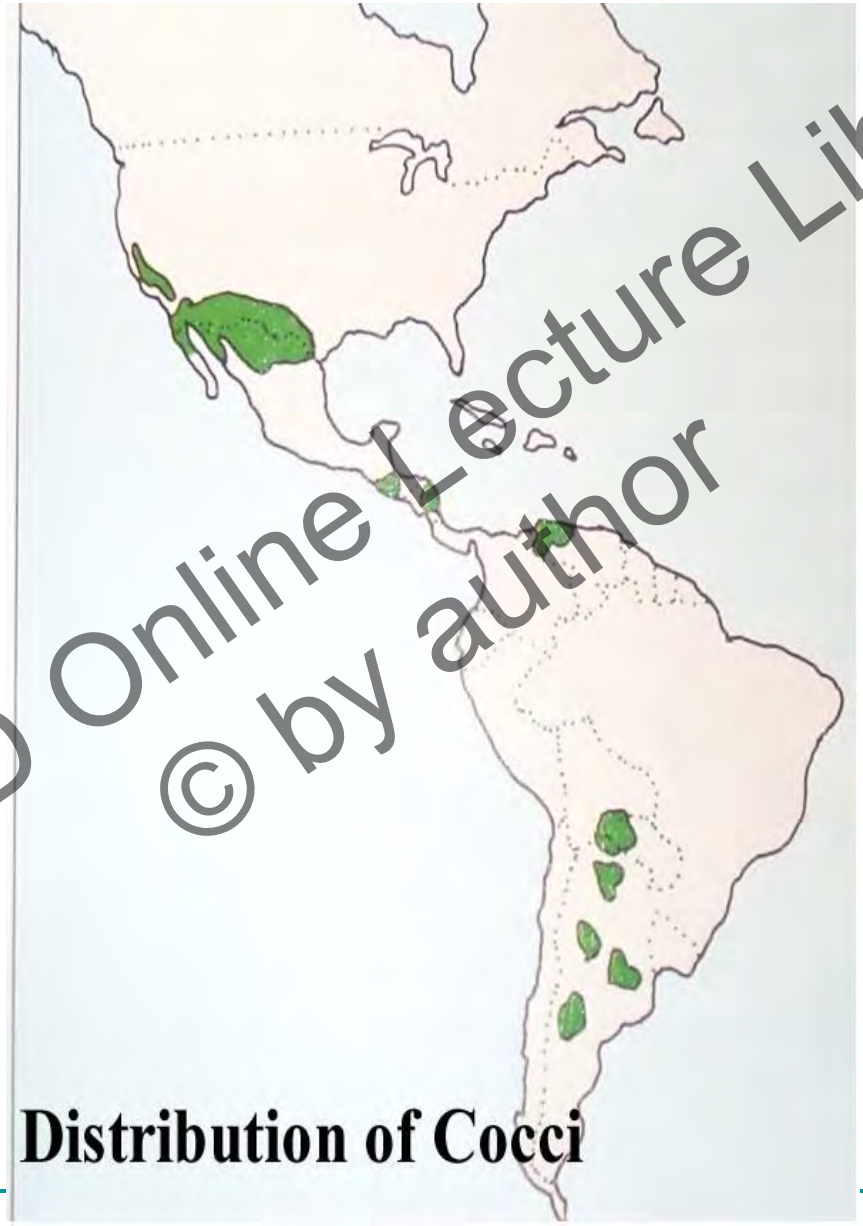
Histoplasmosis

- Histoplasmosis is caused by the dimorphic fungus *Histoplasma capsulatum.*
- increased risk for symptomatic illness
  - Environmental exposure,
  - positive *Histoplasma serology,*
  - *CD4+ count* <150 cells/µL



Coccidioidomycosis

- areas in which the disease is endemic,
  - the Southwestern United States
  - parts of Central and South America
- the risk for developing symptomatic disease in areas in which the disease is endemic increases when:
  - CD4 count is <250 cells/*μL*
  - *with a diagnosis of AIDS*



Distribution of Cocci

Prophylaxis to prevent first episode of opportunistic disease

Pathogen	Indication	First choice	Alternative
Histoplasma capsulatum infection	CD4+ count ≤150 cells/μL and at high risk because of occupational exposure or live in a community with a hyperendemic rate of histoplasmosis (>10 cases/100 patient-years) **(CI)**	Itraconazole 200 mg PO daily **(CI)**	
Coccidioidomycosis	Positive IgM or IgG serologic test in a patient from a disease-endemic area, and CD4+ count <250 cells/μL **(CIII)**	Fluconazole 400 mg PO daily **(CIII)** Itraconazole 200 mg PO bid **(CIII)**	

Varicella-Zoster Virus Diseases

- Approximately 95% of adults have had varicella
- Reactivation of latent VZV results in herpes zoster
- lifetime risk for herpes zoster is 15%–20%,
  - elderly and immunocompromised persons.
- The incidence of herpes zoster is >15-fold higher for HIV-infected adults
- *Herpes zoster can occur in HIV-infected adults at any CD4+ count, but frequency of disease is highest with CD4+ counts of <200 cells/μL*

Varicella-Zoster Virus Diseases

- Pre-exposure prevention:
  - Patients with CD4+ count >200 cells/μL who have not been vaccinated, have no history of varicella or herpes zoster, or who are seronegative for VZV (CIII)
- Primary varicella vaccination (Varivax™),
  - 2 doses (0.5 mL SQ) administered 3 months apart

Varicella-Zoster Virus Diseases

- Post-exposure – close contact with a person who has active varicella or herpes zoster:
- For susceptible patients (those who have no history of vaccination or of either condition, or are known to be VZV seronegative) (AIII)
  - Varicella-zoster immune globulin IM, administered within 96 hours after exposure to a person with active varicella or herpes zoster (AIII)

Cytomegalovirus

- disseminated or localized end-organ disease
- Usually reactivation
- End-organ disease: CD4+ <50 cells/µL
- Clinical Manifestations (before ART)
  - Retinitis 30%
  - Colitis 5-10%
  - Esophagitis 5%

Preventing Disease

- CMV end-organ disease is best prevented using ART to maintain the CD4+ count >100 cells/μL.
- oral valganciclovir would likely prevent the occurrence of CMV retinititis
  - when CD4+ counts <50 cells/μL,

Preventing CMV Disease

- Prophylaxis is not usually recommended
  - cost
  - potential to induce CMV resistance
  - the utility of treating disease when it occurs
  - lack of demonstrated survival advantage

Preventing CMV Disease

- The primary method for preventing severe CMV disease is recognizing the early manifestations of the disease.
- Patients should be made aware of
  - Be aware of the floaters in the eye
  - assess their visual acuity regularly by using simple techniques (e.g., reading newsprint).
  - Regular funduscopic examinations

Human papillomavirus infection

- HPV a common sexually transmitted DNA virus
- *The most frequent cause of cervical cancer.*
- *Most HPV infections, resolve or become latent and undetectable*
- *persistent infection with an oncogenic HPV type is required for tumorigenesis.*
- *Of more than 100 HPV types,*
  - *more than 40 can infect the cervix,*
    - *13 of these are considered oncogenic types,*

HPV infection and HIV

- HIV seropositivity is associated with
  - a high prevalence of HPV infection,
  - low-grade cervical intraepithelial neoplasia (CIN)
  - the precursor to cervical cancer, CIN 3

HPV infection and HIV

- After obtaining a complete medical history, including the history of previous cervical disease, HIV-seropositive women should have a pelvic examination and a Pap test.
- The Pap test should be obtained twice during the first year after diagnosis of HIV infection and, if the results are normal, annually thereafter **(AII).**

HPV vaccine and HIV

- No data are available regarding the safety, tolerability, immunogenicity, or efficacy in HIV-infected women
- HPV vaccine is not absolutely contraindicated in HIV-seropositive women, and it may be used in circumstances when the clinician believes clinical benefit can be derived

Hepatitis A virus (HAV) infection

- HAV-susceptible patients with chronic liver disease, or who are injection-drug users, or men who have sex with men (AII).

Hepatitis B virus (HBV) infection

- All HIV patients without evidence of prior exposure to HBV should be vaccinated with HBV vaccine, including patients with CD4+ count <200 cells/μL (AII)

WHEN TO DISCONTINUE PROPHYLAXIS

Pneumocystis pneumonia (PCP)

- Discontinue prophylaxis
  - CD4+ count >200 cells/μL for >3 months in response to antiretroviral therapy (ART)(AI)
- Restart prophylaxis
  - CD4+ count <200 cells/μL (AI)

Toxoplasma gondii encephalitis (TE)

- Discontinue prophylaxis
  - CD4+ count >200 cells/μL for >3 months in response to ART (AI)
- Restart prophylaxis
  - CD4+ count <100–200 cells/μL (AIII)

Disseminated Mycobacterium avium complex (MAC) disease

- Discontinue prophylaxis
  - CD4+ count >100 cells/μL for >3 months in response to ART (AI)
- Restart prophylaxis
  - CD4+ count <50 cells/μL (AIII)

Histoplasma capsulatum infection

- Discontinue prophylaxis
  - If used, CD4+ count >150 cells/μL for 6 months on ART (BIII)
- Restart prophylaxis
  - For patients at high risk for acquiring histoplasmosis, restart at CD4+ count <150 cells/μL (CIII)

Coccidioidomycosis

- Discontinue prophylaxis
  - CD4+ count >250 cells/μL for >6 months (CIII)
- Restart prophylaxis
  - CD4+ count <250 cells/μL (BIII)

THANK YOU