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Opportunistic Infections

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Learning Objectives

- Utilize current indications when prescribing medications for the primary prevention of OIs
- Recognize the most common presenting signs and symptoms for selected OIs and order appropriate diagnostic studies and treatment
- Implement current vaccine recommendations for individuals who are infected with HIV
- Identify evidence-based resources and access current information on these topics



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Opportunistic Infections

- Infections that are more frequent or more severe because of immunosuppression in persons living with HIV
- Early 1990s, chemoprophylaxis, immunizations, and improved management of acute OIs →→ improved QOL and survival
- Mid-1990s the ART era →→ profound reduction in OI-related mortality

Centers for Disease Control and Prevention. Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Infected Adults and Adolescents. MMWR 2009; 58(No. RR-4).



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OIs continue to cause considerable mortality and morbidity...

- Many patients are unaware of their HIV infection and seek medical care when an OI becomes the initial indicator of their disease
- Certain patients are aware of their HIV infection, but do not take ART because of psychosocial or economic factors
- Certain patients fail to attain adequate virologic and immunologic response on ART because of factors related to adherence, pharmacokinetics, or unexplained biologic factors



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Complications with CD4 Cell Counts

CD4 Cell Count	Infectious Complications
200-500 cells/mm ³	Pneumococcal and other bacterial pneumonias Pulmonary tuberculosis Herpes zoster Oropharyngeal candidiasis Cryptosporidiosis, self-limited Kaposi sarcoma Oral hairy leukoplakia
<200 cells/mm ³	Pneumocystis pneumonia Disseminated histoplasmosis and coccidioidomycosis Miliary/extrapulmonary TB Progressive multifocal leukoencephalopathy (PML)



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Complications with CD4 Cell Counts

CD4 Cell Count	Infectious Complications
<100 cells/mm ³	Disseminated herpes simplex Toxoplasmosis Cryptococcosis Cryptosporidiosis, chronic Microsporidiosis Candidal esophagitis
<50 cells/mm ³	Disseminated cytomegalovirus Disseminated Mycobacterium avium complex



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Mr. Michaels is a 26 y.o. AA heterosexual male

- Recently admitted to your clinic after being diagnosed with HIV during an STD clinic visit.
- Initial lab work:
 - CMP & CBC normal
 - CD4 of 128 cells/ul (repeat 120 cells/mm³)
 - HIV-RNA viral load of 450,000
 - RPR negative
 - Toxo IgG +, Hep A Total Ab+, Hep C Ab+
 - Hep BsAg-, Hep B sAb-, Hep B cAb-



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Primary and Secondary Prophylaxis against OIs

- Primary prophylaxis-- treatment given to HIV infected individuals to **prevent a first episode** of an OI
- Secondary prophylaxis or maintenance therapy-- treatment given to HIV-infected individuals to **prevent a recurrence** of the infection
- Primary prophylaxis is recommended to prevent 3 important OIs: *Pneumocystis jirovecii* pneumonia (PCP), *Mycobacterium avium* complex (MAC), and toxoplasmosis.



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OI Primary Prophylaxis

Indication	Infection	Preferred Regimen	Stop Prophy
CD4 < 200 cells/mm ³ OR Hx of thrush OR CD4% <14 OR Any AIDS-defining illness	<i>Pneumocystis jirovecii</i> pneumonia (PCP)	TMP-SMZ-DS 1 po daily OR TMP-SMZ-SS 1 po daily	On ART with CD4 > 200 cells/mm ³ for ≥ 3 months
CD4 <100 cells/mm ³ and toxoplasma IgG+	<i>Toxoplasma gondii</i> encephalitis	TMP-SMZ-DS 1 po daily	On ART with CD4 > 200 cells/mm ³ for ≥ 3 months
CD4 <50 cells/mm ³ after ruling out active MAC infection by clinical assess with or w/out blood culture	Disseminated <i>Mycobacterium avium</i> complex (MAC) disease	Azithromycin 1200 mg po weekly OR clarithromycin 500 mg po BID	On ART with CD4 >100 cells/mm ³ for ≥ 3 months



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Mr. Michaels is a 26 y.o. AA heterosexual male

- Recently diagnosed with HIV at an STD clinic where he was also diagnosed with GC
- Initial lab work revealed:
 - CMP & CBC normal
 - CD4 of 120 cells/mm³
 - HIV-RNA viral load of 450,000 copies/mL
 - RPR negative
 - Toxo IgG +, Hep A Total Ab-, Hep C Ab-
 - Hep BsAg-, Hep B sAb-, Hep B cAb-



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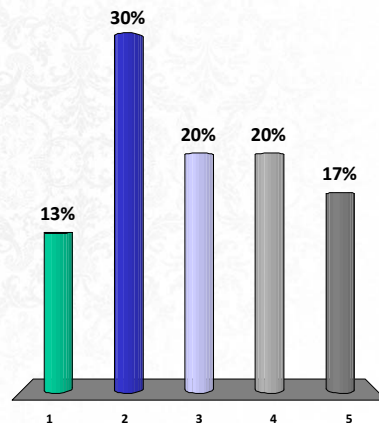
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For what infections will Mr. Michaels need primary prophylaxis?

1. **PCP**
2. Toxoplasmosis
3. MAC
4. 1 and 2
5. none



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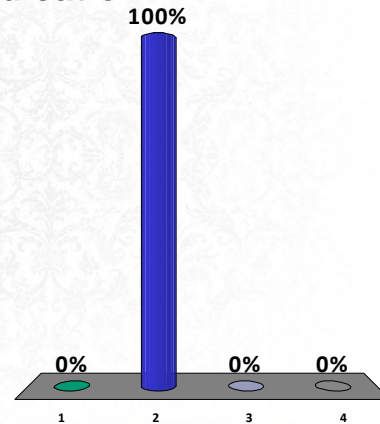
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Mr. Michael's TMP-SMZ DS was stopped after 3 days because of a significant rash.
What would be your likely alternative prophylactic medication?

1. TMP-SMX SS
2. Dapsone
3. Leucovorin
4. Atovaquone



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Diagnosis of Common OIs

- Epidemiology & Etiology
- Clinical Manifestations: Signs and symptoms
- Diagnostic Studies
- Common Differential Diagnoses



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Pneumocystis jiroveci **aka: *Pneumocystis carinii* pneumonia & PCP**

- **Epidemiology & Etiology**
 - Caused by an unusual fungus
 - Common asymptomatic infection in childhood
 - Clinical illness occurs only in the presence of advanced immunosuppression



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PCP: Clinical Manifestations

- **Clinical Manifestations**
 - Fever
 - Night sweats
 - SOB, particularly with exertion
 - Nonproductive cough
 - Weight loss
 - Fatigue



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PCP: Differential Diagnoses

- Pneumococcal pneumonia or other pneumonias
- Tuberculosis
- *Mycobacterium avium* complex
- Lymphocytic interstitial pneumonitis
- Bronchitis, Asthma,
- CMV pneumonitis
- Histoplasmosis or other fungal pneumonias, especially *Cryptococcus*
- Pulmonary Kaposi sarcoma
- Congestive heart failure
- Pulmonary hypertension



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Imaging

- **CXR: various presentations**
 - May be normal in early disease
 - Typical: diffuse bilateral, symmetrical interstitial infiltrates
 - May see atypical presentations, including nodules, asymmetric disease, blebs, cysts, pneumothorax
 - Cavitation, intrathoracic adenopathy, and pleural effusion are uncommon (unless caused by a second concurrent process)

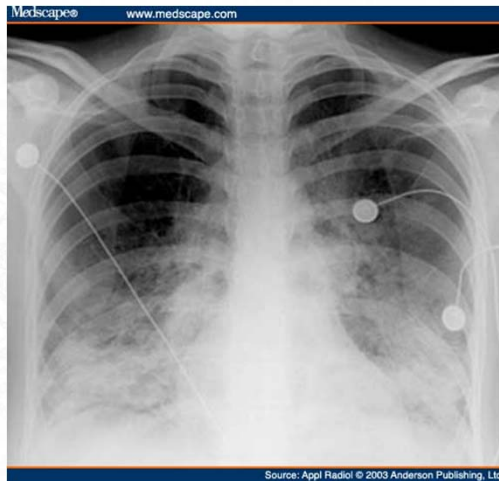


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Imaging



<http://img.medscape.com/fullsize/migrated/461/046/ar461046.fig2a.jpg>



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Definitive Dx of PCP

- **Requires demonstrating organism:**
 - Induced sputum
 - sensitivity <50% to >90%
 - Spontaneously expectorated sputum
 - low sensitivity
 - Bronchoscopy with bronchoalveolar lavage
 - sensitivity 90-99%
 - Transbronchial biopsy
 - sensitivity 95-100%
 - Open-lung biopsy
 - sensitivity 95-100%



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Toxoplasmosis

- **Epidemiology & Etiology**
 - Primary infection acquired from tissue cysts in undercooked meat or ingestion of sporulated oocysts (from cat feces) in soil, water, or food
 - No transmission by person-to-person contact



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Toxoplasmosis

- **Clinical Manifestations**
 - Focal encephalitis with headache, confusion, or motor weakness and fever
 - Focal neurological abnormalities, may progress to seizures, altered mental status, coma
 - Dissemination may occur (rarely), with retinochoroiditis, pneumonia, other organ involvement



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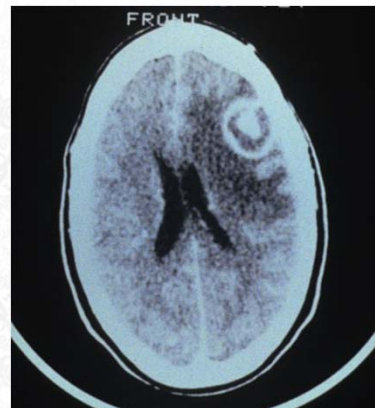
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Toxoplasmosis

- **Definitive Dx:**
 - Compatible clinical syndrome + imaging + detection of organism in a clinical sample (brain biopsy)
 - Imaging: CT, MRI of brain: typically reveal multiple contrast-enhancing lesions, often with edema
 - PET or SPECT may help distinguish TE and lymphoma
- **Differential Dx:**
 - CNS lymphoma, mycobacterial infection (TB), fungal infection, Chagas disease, abscess, PML

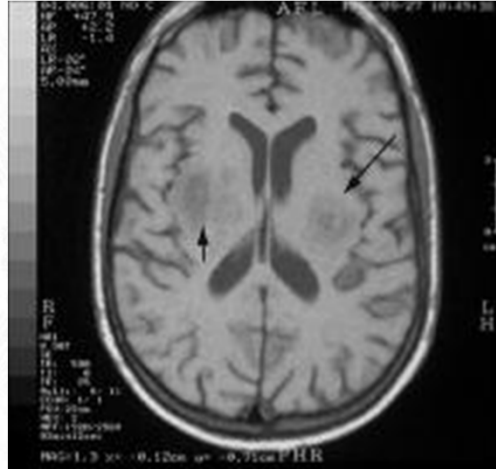
Imaging

CT scan of the brain
showing contrast-enhancing
lesion of toxoplasmosis



P. Volberding, MD, UCSF Center for HIV Information Image Library

Imaging



<http://emedicine.medscape.com/article/344706-overview>



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Mycobacterium Avium Complex

- **Epidemiology & Etiology**
 - Ubiquitous in the environment & transmission believed to be via inhalation, ingestion, inoculation via respiratory or GI tract;
 - Person-person transmission unlikely
 - Not associated with specific environmental exposures or behaviors
 - Risk factors: plasma HIV RNA >100,000 copies/mL, previous opportunistic infections, previous colonization with MAC



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MAC

- **Clinical Manifestations:**

- Persistent or cyclic fever
- Night sweats
- Unintentional weight loss
- Anorexia
- Chronic diarrhea
- Fatigue & Weakness
- Abdominal pain



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MAC

- **Diagnostics:**

- A definitive diagnosis requires isolation of MAC from the blood or other normally sterile body fluids or tissues
- Send blood for acid-fast bacilli (AFB) culture (2-3 samples)

- **Differential Diagnoses:**

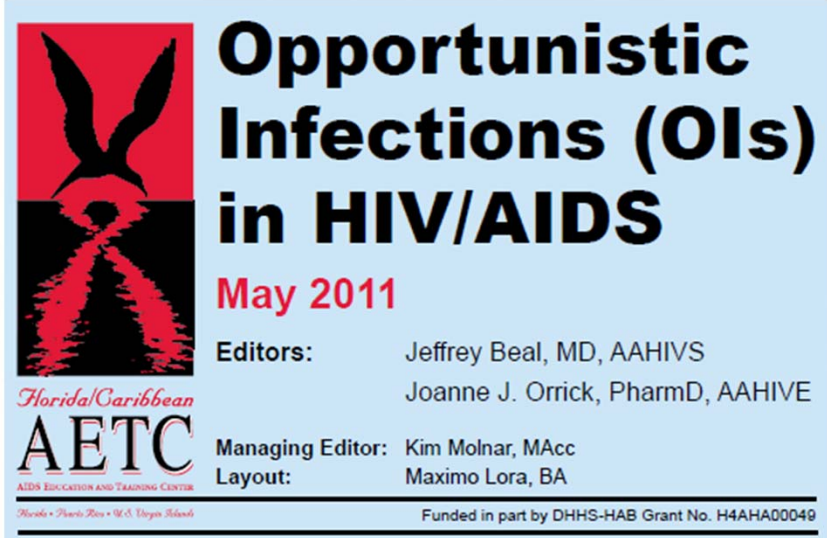
- *Mycobacterium tuberculosis*
- Cytomegalovirus; Lymphoma; *Bartonella*
- Disseminated fungal infection
- Pyogenic abscess or other septicemia



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Opportunistic Infections (OIs) in HIV/AIDS
May 2011

Editors: Jeffrey Beal, MD, AAHIVS
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Mr. Michaels

- After switching his PCP prophylaxis med from TMP-SMZ to Dapsone and subsequent resolution of his rash, Mr. Michaels had no additional problems with his meds.
- Additional conversations with his RN care coordinator at the end of weeks 2 and 3 suggested good adherence to his medications without any additional side effects
- F/u labs at 4 weeks: CD4=170 cells/mm³ and HIV VL 32,000 copies/mL

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At week 8, Mr. Michaels developed a headache and slight dizziness

- Afebrile, BP 145/86, pulse 90, pain 7/10
- He says he just “isn’t thinking clearly”. His wife states he was “tossing & turning alot during the night and just doesn’t seem himself”.
- Pupils OS=3mm & brisk OD=4mm & sluggish
- 911 was called and he was transported to ER
- Brain CT revealed several ring-enhancing lesions with mild cerebral edema.



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Dx: Toxoplasmosis (IRIS)

- First-line preferred drugs for treatment of toxo were started: Pyrimethamine + sulfadiazine + leucovorin
- His symptoms resolved at approximately 10 days and his MRI showed improvement of the lesions
- He was treated for 6 weeks at which time he was asymptomatic and the CT of his brain was clear.
- Reduced doses of his 3 meds were continued as maintenance therapy

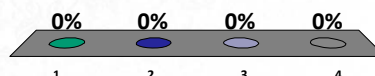


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When can Mr. Michaels' secondary prophylaxis be discontinued?

1. If successfully completed treatment
2. If asymptomatic
3. If CD4 >200 for >6 months
4. All of the above



Adult Immunizations for Persons with HIV: MMWR, 2011

VACCINE	CD4 <200 cells/ul	====	CD4 >200 cells/ul
Influenza	1 dose annually (totally inactivated vaccine)		
Pneumococcal	1 or 2 doses		
Hepatitis A (if seronegative)	2 doses		
Hepatitis B (if seronegative)	3 doses		

Adult Immunizations for Persons with HIV: MMWR, 2011

VACCINE	CD4 <200 cells/ul	====	CD4 >200 cells/ul
Tetanus, diphtheria, pertussis (Td/Tdap)	Substitute 1-time dose of Tdap for Td booster; then boost Td every 10 years		
Varicella	Contraindicated	====	2 doses
Human papillomavirus (HPV)	3 doses through age 26		
Zoster	Contraindicated	====	no recommendation
Measles, mumps, rubella	Contraindicated	====	1 or 2 doses
Meningococcal	1 dose for unvaccinated college students living in dormitories, military recruits, persons who travel to hyperendemic areas (sub-Saharan Africa)		

MMWR/ Feb. 4, 2011/ Vol. 60. No. 4

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Influenza Vaccine

- Recommended annually
- Vaccination is most effective among persons with CD4 counts of >100 cells/ μ L and HIV RNA viral loads of <30,000 copies/mL
- In patients with advanced disease and low CD4 cell counts, inactivated vaccine may not produce protective antibodies
 - A second dose of vaccine does not improve response in these patients.
- Live, attenuated cold-adapted influenza vaccine (LAIV, FluMist) is contraindicated for use by patients with HIV infection.

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Pneumococcal Vaccine

- Polysaccharide
- Recommended for all at baseline and 1 booster at 5 years= total 2 per lifetime
- If CD4 count is <200 cells/mm³, may be less effective; revaccinate when CD4 count increases in response to ART



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Hepatitis A Vaccine

- Recommended for persons with chronic liver disease, IDU, MSM, international travelers, and hemophiliacs.
- Serologic response (HAV IgG or Total Ab) should be checked 1 month after completion of series, and nonresponders should be revaccinated. 2 doses (0, 6-12 months).



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Hepatitis B Vaccine

- Many experts recommend a high dose (40 mcg) of HBV vaccine. This is the standard for hemodialysis patients.
- Standard dosing schedule is 3 doses (0, 1, and 6 months).
- If 40 mcg is given, the recommended schedule is 3 doses of Recombivax HB at 0, 1, and 6 months or 4 doses of Engerix-B at 0, 1, 2, and 6 months.
- Anti-HBV surface Ab titers should be checked 1 month after completion of vaccine series. Patients whose titer level is ≤ 10 should be revaccinated. (series X 1)



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Hepatitis B Vaccine

- **Most HIV-infected patients with isolated HBV core Ab+ (without HBV viremia) are not immune and should receive a complete series of HBV vaccine.**
- **Some specialists recommend that HIV-infected patients with isolated HBV core Ab+ be tested for HBV DNA prior to immunization.**



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Recalling Mr. Michael

- **Recalling Mr. Michael's Initial lab work:**
 - CMP & CBC normal
 - CD4 of 120 cells/mm³
 - HIV-RNA viral load of 450,000 copies/mL
 - RPR negative
 - Toxo IgG +, Hep A Total Ab+, Hep C Ab+
 - Hep BsAg-, Hep B sAb-, Hep B cAb-



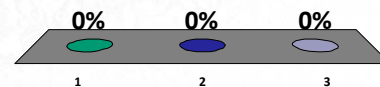
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**Based on Mr. Michael's Hepatitis serology,
what vaccine should be ordered?**

1. Hep A
2. **Hep B**
3. TwinRx



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QUESTIONS

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