HIV Opportunistic Infections in the new era of HAART

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Infectious Disease

- In the United States, the incidence of HIV-associated opportunistic infections (OIs) has decreased dramatically.
- These reductions have resulted, in part, from improvements in and the diffusion of effective OI prophylaxis, but most importantly, they have resulted from the advent of combination antiretroviral therapy.
- As antiretroviral therapy becomes simpler, more potent, and less toxic, and as our clinical concerns focus increasingly on the growing number of non–HIV-associated complications of HIV infection, we might be falsely reassured that OIs are soon to become a thing of the past.


Scenarios

- Pts who are unaware that they have HIV infection: OI as the initial indicator of late-stage disease
- Patients who remain unlinked to care or, if receiving care
- Patients receiving care and who, on HAART do not attain adequate virologic and immunologic response because of poor adherence to therapy, extensive antiretroviral resistance, or unexplained biological factors

Case 1

- A 28 year old male with HIV (CD4 count unknown) presents to the ER with left sided pneumothorax. He lives in Chicago and has never left the midwest.

The most likely infectious cause of this pneumothorax is:

1. Histoplasmosis
2. Blastomycosis
3. PCP
4. CMV
5. Aspergillosis

PCP

- Pneumocystis carinii pneumonia (PCP, officially renamed Pneumocystis jirovecii pneumonia) is the most common AIDS-defining opportunistic infection (OI) in patients infected with the human immunodeficiency virus (HIV)
- Taxonomy: based upon analysis of its ribosomal and mitochondrial DNA suggesting a close resemblance to fungi. It does not respond to antifungal therapy nor grows on fungal media, many experts feel it is not a true fungus

- several studies highlight that PCP still occurs even in patients receiving HAART and is still a major cause of death in AIDS patients in the United States
- Occasional cases can be anticipated when PCP prophylaxis is discontinued with immune reconstitution and a CD4 count >200 cells/microL
Susceptibility to PCP

- CD4 < 200 cells/mL
- CD4% < 15
- Oral thrush
- Prior PCP
- Prior pneumonia (or recurrent)
- Unexplained fever > 101 F

Distribution of CD4 Counts Measured within 4 months of PCP (N=24, 924 followed by 8 months) Chu et al JAMA

<table>
<thead>
<tr>
<th>CD4</th>
<th>% PCP Dx</th>
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<tr>
<td>300 or more</td>
<td>5.5%</td>
</tr>
<tr>
<td>200-299</td>
<td>5.6%</td>
</tr>
<tr>
<td>50-199</td>
<td>34.5%</td>
</tr>
<tr>
<td>0-49</td>
<td>54.4%</td>
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Clinical Features of PCP

- Dyspnea
- Fever
- Cough
  - productive
  - non productive
- Chest pain
- Cyanosis
- Rales

Diagnosis of PCP

- LDH: sensitivity depends on severity of pulmonary disease. Non-specific
- Chest CT: ground glass appearance is nonspecific (Diffuse symmetric interstitial infiltrates vs lobar infiltrates, pneumothorax, cavitary lesions, solitary nodules infiltrate with effusion and NORMAL Chest xray).
- Pulmonary function tests DLCO: not specific
- Gallium Scan: not specific

The figure is derived from an analysis of a bronchoalveolar lavage fluid (BALF) sample taken from a patient with Pneumocystis pneumonia (PCP) (an adult HIV-1-infected male). Trichomonad cells (Tr) can be identified in the vicinity of an aggregate of Pneumocystis (Pc) and macrophages (Ma). The stain used was May Grünwald Giemsa 1,000. The scale bar represents 10 m. Other photomicrographs of samples taken from other patients with PCP (from the same and other institutions).
Treatment of Pneumocystis pneumonia

- In patients who can tolerate the regimen, treatment with trimethoprim-sulfamethoxazole (TMP-SMX) is the initial drug of choice for both intravenous and oral therapy
- Prior prophylaxis — The occurrence of PCP in patients who are compliant with TMP-SMX prophylaxis is highly unusual
- breakthrough PCP in patients receiving prophylaxis with dapsone, atovaquone, or aerosolized pentamidine is relatively more common

Intravenous therapy

- wide A-a gradient (above 45 mmHg)
- poor oxygenation (partial pressure of arterial oxygen below 60 mmHg)
- or potential for fatigue leading to respiratory failure
- When oral treatment cannot be administered because of clinical status or gastrointestinal issues (such as severe esophageal candidiasis)
- In patients who require pentamidine (usually because of multiple drug intolerances)

Oral versus intravenous therapy

- Patients who have mild disease not requiring corticosteroids can receive oral anti-pneumocystis therapy
- Even for patients with moderate disease severity oral therapy is still a reasonable option, as many of the regimens (TMP-SMX, TMP-dapsone, clindamycin-primaquine) have excellent oral absorption

**PCP TREATMENT SIDE EFFECTS**

- TMP-SMX: Rash, hepatotoxicity, neutropenia (tx with G-CSF), high-dose therapy often causes hyperkalemia, since trimethoprim acts as a potassium sparring diuretic
- Adverse effects seen with TMP-SMX in patients with HIV infection are dose related. May still be able to tolerate the much lower dose used for PCP prophylaxis
PCP TREATMENT SIDE EFFECTS

- TMP-dapsone — gastrointestinal upset, rash, hemolytic anemia, and methemoglobinemia.
- Patients should be tested for G6PD deficiency when initiating therapy with dapsone. Therapy may be started before the results of the test are available.
- Oral clindamycin-primaquine — Side effects include rash, hemolytic anemia, neutropenia, methemoglobinemia, diarrhea, and Clostridium difficile-associated colitis.

PCP TREATMENT SIDE EFFECTS: PENTAMIDINE

- Adverse reactions occur in up to 70 percent of patients and include nausea, taste disturbance, cardiac arrhythmias, hyperkalemia, nephrotoxicity, pancreatitis, hypokalemia, hypoglycemia, and hyperglycemia. Patients can develop permanent insulin-requiring diabetes mellitus after treatment with pentamidine.
- The nephrotoxicity of pentamidine is cumulative and is usually evidenced by a gradual increased in the creatinine concentration over the course of therapy.
- The drug should be given while the patient is supine, adequately hydrated, and administered over at least 60 minutes. Hepatitis and bone marrow suppression also occur.

Prognosis

- Increasing age
- Prior episodes of PCP
- Elevated serum lactate dehydrogenase concentration
- Low CD4 cell count
- The presence of cytomegalovirus in bronchoalveolar lavage fluid

HAART and PCP treatment

- The appropriate time to initiate antiretroviral therapy (ART) in patients with PCP who are not already on such therapy is not clear.

Potential risks of ART in this setting include drug-drug interactions, overlapping toxicities, increased pill burden, and the potential for eliciting an immune reconstitution illness.

Starting ART offers potential clinical benefits that counter these concerns in the treatment-naive patient. We recommend initiation of ART within two weeks of PCP treatment.

In the patient already on ART, we advise continuation of antiretroviral medications.

Case 2

- A 29 yo woman who is a hospital worker comes to see you because of fever and marked dyspnoea. Her husband had died of AIDS 2 years ago, but she has never sought evaluation out of fear.
- You order sputum times 3 for AFB and a chest X-ray.
- You order an HIV test.
Case 2
- The initial chest X-ray is interpreted as normal
- 3 smears are AFB negative
- Her HIV test is + and the CD4 count is 26
- She remains febrile and short of breath (SOB)

Q1: What would you do?

Case 2
- Empiric trial of PCP and CAP treatment started
- 5 days later she is much worse
- A repeat X-ray now shows diffuse reticular-nodular infiltrates throughout the lungs, with a miliary pattern

Q2: What is your next step?

Case 2
- Patient is started on a standard anti-TB treatment regimen while sputum cultures pending
- She gradually improves. She continues TMP-SMX in preventive dosage and ART is started
- Sputum culture results are available after 4 weeks and are positive for *M. tuberculosis* complex

The Effects of TB on HIV Progression
- TB increases HIV progression
- Dually infected persons often have very high HIV viral loads
- Immuno-suppression progresses more quickly, and survival may be shorter despite successful treatment of TB
- co-infected pts have a shorter survival period than persons with HIV who never had TB disease

The Effects of Immune Suppression on TB Progression
- HIV+ person has a greater risk of reactivation of latent TB infection (LTBI)
- HIV+ person is more likely to progress to TB disease following infection
- HIV+ person has a high risk of becoming sick again after treatment
- HIV+ person with LTBI has a 5-10% annual risk of developing active TB (versus 10% lifetime risk among HIV-negative persons)

Clinical Presentation of HIV-related TB
- **CD4 counts >350**
  - Disease usually limited to the lungs
  - Often presents like TB in HIV-uninfected persons
  - “typical” chest X-ray findings with upper lobe infiltrates with or without cavities
- **CD4 counts <50-100**
  - Extrapulmonary disease is common
  - Disseminated disease with high fevers and rapid progression is seen
  - Chest X-ray findings often look like “primary TB” with adenopathy, effusions, interstitial or miliary

Diagnosing TB in Persons with HIV

- In HIV-positive or suspect patients:
  - 3 sputum samples for microscopy are indicated for any symptoms of TB regardless of duration or sputum characteristics
  - Fever and weight loss can be important symptoms
  - If sputum smear is +, a chest X-ray is not required to confirm the diagnosis PTB

Primary Pulmonary TB and adenitis

HIV/TB co-infection treatment

- For HIV-infected patients newly diagnosed with TB, six months of therapy is probably adequate in most situations
- However, prolonged therapy (up to nine months) is recommended for patients with a delayed clinical or bacteriological response to therapy (e.g., symptomatic or positive culture results at or after two months of therapy) and sometimes also for patients with cavitary disease on chest radiograph
- MMWR March 24, 2009 / 58(Early Release):1-198

Post primary TB: cavitation and consolidation

Pattern of TB and Survival of Patients with HIV-related TB

HIV/TB co-infection treatment

- Once or twice-weekly dosing has been associated with an increased rate of acquired rifamycin resistance among patients with advanced HIV disease (CD4+ T cell counts of <100 cells/mm³)
- Once-weekly rifapentine is contra-indicated in HIV-infected patients
- Additionally, it is recommended that RIF- and rifabutin-based regimens be given at least three times weekly for patients with TB and advanced HIV disease (CD4+ T cell counts of <100 cells/mm³)
### Treatment of TB for HIV-Positive

- Rifampicin-based regimens generally recommended for persons
  - Those who have not started antiretroviral therapy
  - For whom rifampicin-incompatible PIs or NNRTI-based regimens are not essential
- Initial treatment phase should consist of:
  - Isoniazid (INH)
  - Rifampicin (RIF)
  - Pyrazinamide (PZA)
  - Ethambutol (EMB)
- RIF may be used with some PIs and NNRTIs

### Treatment of TB for HIV-Positive

- For patients receiving PIs or NNRTIs, initial treatment phase may consist of:
  - Isoniazid (INH)
  - Rifabutin (RFB)
  - Pyrazinamide (PZA)
  - Ethambutol (EMB)
- An alternative non-rifamycin regimen includes INH, EMB, PZA, and streptomycin (SM) but is not generally recommended

### Rifampicin Decreases Blood Levels of Nevirapine and Efavirenz

<table>
<thead>
<tr>
<th>NNRTI</th>
<th>Effect of rifampicin on NNRTI</th>
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<tbody>
<tr>
<td>Nevirapine (NVP)</td>
<td>↓ 37-58%</td>
</tr>
<tr>
<td>Efavirenz (EFV)</td>
<td>↓ 13-26%</td>
</tr>
</tbody>
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### Rifampicin Markedly Decreases Blood Levels of all PIs

<table>
<thead>
<tr>
<th>Protease Inhibitor</th>
<th>Effect of rifampicin on PI</th>
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<tbody>
<tr>
<td>Saquinavir</td>
<td>↓ by 80%</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>↓ by 35%</td>
</tr>
<tr>
<td>Indinavir</td>
<td>↓ by 90%</td>
</tr>
<tr>
<td>Nelfinavir</td>
<td>↓ by 82%</td>
</tr>
<tr>
<td>Amprenavir</td>
<td>↓ by 81%</td>
</tr>
<tr>
<td>Lopinavir/ritonavir</td>
<td>↓ by 75%</td>
</tr>
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### HAART and Rifampicin-Based TB Therapy

- Recommended regimen: **efavirenz plus 2 nucleosides**
  - Use EFV for adults and children >3 years old
  - Avoid 1st trimester of pregnancy
  - Other options:
    - **Nevirapine (NVP) plus 2 NRTIs**
      - Some successful clinical experience in Spain
      - Persistent worry about low blood levels
      - Some suggest increasing NVP to 300 mg twice-daily
      - Preferred alternative in children < 3 years of age

### Treatment Options: ART During Rifampicin-Based TB Therapy

- Ritonavir boosting of other PIs can achieve adequate blood levels but has hepatotoxicity
  - Lopinavir/ritonavir (Kaletra) usual dose 2 tabs bd PLUS an extra ritonavir 300 mg bd
  - Can be used in children
**When to Start ART During TB Therapy?**

- HIV-infected TB patients should be evaluated for ART immediately
- CD4 <200 - start ART between 2-8 weeks after start of anti-TB therapy
- CD4 >200 but <350 - start ART 8 weeks after start of anti-TB therapy
- CD4 ≥350 - defer ART but re-evaluate at 8 wks and at end of anti-TB therapy
- HIV-infected patients already on ARVs who develop TB should begin anti-TB meds immediately

**TB and AIDS**

- TB is an AIDS-defining illness and is therefore an indication for initiation of ART.
- Issues about HAART and TB treatment:
  - Identification of patients who will benefit from antiretroviral therapy
  - Drug-drug interactions
  - Immune reconstitution events
  - Overlapping ARV and TB medicine side effect
  - Adherence with multi-drug therapy for two diseases
  - Coordinating care between TB and HIV care providers

**Case 3**

42 year old lady (HIV positive) was admitted with pulmonary congestion, fever 38 C and headache for the last six weeks and neck rigidity for the last fifteen days

Wet mount, Gram staining and India ink preparation of the CSF showed 4-7µm, round budding yeast cells with capsule. 5-6 lymphocytes were also seen per high power field.

**Cryptococcus neoformans and AIDS**

- begins in the lungs
- meningoencephalitis is the most frequently encountered manifestation of cryptococcosis in patients with HIV
- It rarely occurs in patients with CD4 T-lymphocyte counts greater than 100/µL
- Typically the burden of organisms is generally higher and the inflammatory response is much less than in non-AIDS patients with this infection

**Symptoms and PE Cryptococcus and AIDS**

indolent fashion (over a period of one to two weeks)
fever, malaise, and headache
Stiff neck, photophobia, and vomiting are only seen in one-fourth to one-third of patients
Other symptoms, suggesting disseminated disease, may be present including cough, dyspnea, and skin rash Clinical disease is rarely fulminant, in which case the patient may present with coma with rapid progression to death.

**Disseminated skin infection**

- PE is unimpressive. 24% : AMS on presentation and only 6% present with focal neurologic deficits
- disseminated disease may be evident, including tachypnea and skin lesions resembling molluscum contagiosum. Visual and hearing loss have also been reported
### Cryptococcocal ME Dx

- Cryptococcal antigen is almost invariably detected in CSF at high titer in patients with meningitis or meningoencephalitis
- The serum cryptococcal antigen is also almost always positive in cases of CNS disease and in other instances of disseminated infection
- Up to 75% of patients with HIV-associated cryptococcal meningitis have routine blood cultures positive for *C. neoformans*

### Preventing Disease

- Prospective, controlled trials indicate that fluconazole and itraconazole can reduce the frequency of primary cryptococcal disease among patients who have CD4+ counts <50 cells/µL
- Recommendation: antifungal prophylaxis not be used routinely to prevent cryptococcosis because of the relative infrequency of cryptococcal disease, lack of survival benefits associated with prophylaxis, possibility of drug interactions, potential antifungal drug resistance, and cost

### Cryptococcal Meningitis Tx

- Amphotericin B deoxycholate, at a dose of 0.7 mg/kg daily, combined with flucytosine, at a dose of 100 mg/kg daily in four divided doses, for ≥2 weeks for those with normal renal function
- Renal function should be monitored closely and the flucytosine dose adjusted appropriately for patients with renal impairment.
- The addition of flucytosine to amphotericin B during acute treatment is associated with more rapid sterilization of CSF

### Lipid formulations of amphotericin B

- Lipid formulations of amphotericin B
- Renal dysfunction during therapy or have a likelihood of having renal failure
- No optimal dose of lipid formulations determined. A dose of 4–6 mg/kg daily for lipid formulations of amphotericin B is recommended
- Fluconazole (400–800 mg daily) combined with flucytosine is an alternative to amphotericin B plus flucytosine, but is inferior to amphotericin B and is recommended only for persons who are unable to tolerate or unresponsive to standard treatment

### Cryptococcal Meningitis Tx

- After at least a 2-week period of successful induction therapy
- Substantial clinical improvement and a negative CSF culture after repeat lumbar puncture
- Follow-up therapy initiated with fluconazole 400 mg daily. This therapy should continue for 8 weeks. Itraconazole is an acceptable though less effective alternative
- Limited data are available for the newer triazoles, voriconazole and posaconazole, as either primary or follow-up therapy for patients with cryptococcosis. Voriconazole should be used cautiously with HIV PIs and efavirenz

### Increase ICP

- Elevated intracranial pressure (ICP) occurs in more than 50 percent of patients with cryptococcal meningitis and often complicates the management of disease
- Daily lumbar punctures should be performed to reduce the opening pressure to <20 cmH2O or by 50 percent of the initial value. There is no role for acetazolamide, mannitol, or corticosteroids to reduce intracranial pressure
- Lumbar drains can be placed in patients who require frequent spinal taps
CM and AIDS

- ART can be initiated or reinstituted at the end of consolidation therapy.
- Maintenance — After two months of 400 mg/daily, fluconazole dosing can be decreased to 200 mg/day as maintenance therapy.
- Consideration can be given to stopping fluconazole maintenance therapy in selected patients who are asymptomatic, and have responded to HAART with a sustained increase in their CD4+ T lymphocytes for more than a year to greater than 100 cells/microL (and greater than 10 percent CD4).
- These patients should be monitored closely, and fluconazole maintenance reinstituted if the CD4 count falls below 100 cells/microL (and below 10 percent CD4 cells).

MAC and HIV

- Organisms of the Mycobacterium avium complex (MAC) are ubiquitous in the environment.
- The mode of transmission is thought to be through inhalation, ingestion, or inoculation via the respiratory or gastrointestinal tract.
- Person-to-person transmission is unlikely.
- HIV MAC infection usually presents as disseminated disease although localized forms of MAC are being reported with widespread use of more effective antiretroviral therapies.

MAC and HIV

- MAC disease typically occurs among persons with CD4+ counts <50 cells/µL.
- High plasma HIV RNA levels (>100,000 copies/mL)
- Previous OIs, previous colonization of the respiratory or gastrointestinal tract with MAC, and defects in T-cell repertoire.

MAC risk Factors

- Low CD4 count
- Use of an indoor pool for swimming
- Previous bronchoscropy
- Repeated consumption of raw or partially cooked fish or shellfish
- Therapy with granulocyte stimulating factor.

MAC clinical Manifestations

- Early symptoms might be minimal and might precede detectable mycobacteremia by several weeks.
- Fever, night sweats, weight loss, fatigue, diarrhea, and abdominal pain.
- Localized manifestations of MAC disease (pts on ART): cervical or mesenteric lymphadenitis, pneumonitis, pericarditis, osteomyelitis, skin or soft tissue abscesses, genital ulcers, or CNS infection.
Laboratory abnormalities

- particularly associated with disseminated MAC disease include anemia (often out of proportion to that expected for the stage of HIV disease) and elevated liver alkaline phosphatase
- Hepatomegaly
- splenomegaly
- lymphadenopathy
- IRIS, initially characterized by focal lymphadenitis with fever, indistinguishable from active MAC infection

Diagnosis

- clinical signs and symptoms coupled with the isolation of MAC from cultures of blood, lymph node, bone marrow, or other normally sterile tissue or body fluid
- Species identification should be performed using specific DNA probes
- Other ancillary studies: AFB smear and culture of stool or tissue biopsy material

MAC prophylaxis

- CD4+ count of <50 cells/µL Primary MAC prophylaxis should be discontinued among adult and adolescent patients who have responded to ART with an increase in CD4+ counts to >100 cells/µL for ≥3 months
- Azithromycin or clarithromycin are the preferred prophylactic agents
- If azithromycin or clarithromycin cannot be tolerated, rifabutin is an alternative prophylactic agent for MAC disease, although drug interactions might complicate the use of this agent
- R/o active MAC disease and because treatment with rifabutin could result in RIF resistance among persons who have active TB, active TB also should be excluded before rifabutin is used for prophylaxis.

MAC Treatment

- Initial treatment of MAC disease should consist of two or more antimycobacterial drugs to prevent or delay the emergence of resistance
- Clarithromycin is the preferred first agent it has been studied more extensively than azithromycin in patients with AIDS and appears to be associated with more rapid clearance of MAC from the blood. Inhibition of CYP450 3A4 by clarithromycin
- Azithromycin can be substituted for clarithromycin when drug interactions
- EMB is the recommended second drug

MAC Treatment

- Some clinicians add rifabutin as a third drug improves survival and this approach reduced emergence of drug resistance in persons with AIDS and disseminated MAC disease.
- The addition of a third or fourth drug should be considered in persons with advanced immunosuppression (CD4+ count <50 cells/µL), high mycobacterial loads (>2 log10 colony forming units/mL of blood), or in the absence of effective ART, settings in which mortality is increased and emergence of drug resistance is most likely
- the third or fourth drug might include an injectable agent such as amikacin or streptomycin

Case 5

- 38 year old white male who was known to have HIV since 1989
- He had been doing reasonably well on anti retro viral therapy given the duration of his illness
- His last Cluster of Differentiation 4+ (CD4+) count done about a month ago was 225/L and his viral load was 51,000 copies/mL
- He initially presented to his primary care doctor with complaints of blurry vision, unsteady gait and frequent falls in the recent past. Computerized Tomography (CT) scan of his head done by his doctor revealed diffuse white matter disease which dictated the need for further diagnostic testing. Serum IgG for Toxoplasma was found to be negative a few years ago.
Case 5

- The patient was admitted to the hospital
- On examination, the patient was afebrile and had essentially stable vital signs
- He had an unsteady gait, a positive Romberg’s sign, decreased plantar reflex on the right and decreased visual acuity in both eyes
- MRI of his head demonstrated MRECL scattered in the white matter of the left frontal lobe, right occipital lobe and left cerebellar.

Serum IgM for Toxoplasma was found to be negative
After contemplation, the patient was started on presumptive treatment for cerebral toxoplasmosis with Pyrimethamine 100 mg Per Oral (PO) q daily and Sulfadiazine 1000 mg POq 6 hrs. Serum tests for Cryptococcal and Histoplasma antigens; blood cultures and Rapid Plasma Reagin (RPR) were negative.

The patient returned to the hospital in two weeks
- His gait and visual disturbances had begun to resolve
- A repeat MRI of the head showed 50%-80% resolution of the Occipital and Cerebellar lesions and near complete resolution of the Frontal lobe lesions

Toxoplasma gondii and HIV
- The differential diagnosis of focal neurological disease in patients with AIDS
- central nervous system (CNS) lymphoma
- mycobacterial infection (especially TB)
- fungal infection (e.g., cryptococcosis)
- Chagas disease
- bacterial abscess
- rarely PML, which can be distinguished on the basis of imaging studies (PML lesions typically involve white matter rather than gray matter, are noncontrast enhancing, and produce no mass effect).
Toxoplasmosis: transmission

Toxo encephalitis Treatment
- pyrimethamine plus sulfadiazine plus leucovorin
- Pyrimethamine penetrates the brain parenchyma efficiently even in the absence of inflammation
- Use of leucovorin reduces the likelihood of the hematologic toxicities associated with pyrimethamine therapy
- The preferred alternative regimen for patients with TE who are unable to tolerate or who fail to respond to first-line therapy is pyrimethamine plus clindamycin plus leucovorin
- TMP-SMX may be considered an option
- No parenteral formulation of pyrimethamine exists; the only widely available parenteral sulfonamide is the sulfamethoxazole component of TMP-SMX plus parenteral clindamycin

Toxo encephalitis: treatment
- atovaquone (with meals or oral nutritional supplements) plus either pyrimethamine plus leucovorin or sulfadiazine or, for patients intolerant of both pyrimethamine and sulfadiazine, as a single agent
- and azithromycin plus pyrimethamine plus leucovorin daily
- clarithromycin plus pyrimethamine
- 5-fluorouracil plus clindamycin
- dapsone plus pyrimethamine plus leucovorin
- and minocycline or doxycycline combined with either pyrimethamine plus leucovorin, sulfadiazine, or clarithromycin

Toxo encephalitis and AIDS
- Acute therapy for TE should be continued for at least 6 weeks, if there is clinical and radiologic improvement
- Longer courses might be appropriate if clinical or radiologic disease is extensive or response is incomplete at 6 weeks. CNS lesions must not have contrast enhancement on CT/MRI
- Adjunctive corticosteroids (e.g., dexamethasone) should be administered to patients with TE when clinically indicated only for treatment of a mass effect associated with focal lesions or associated edema

Toxo encephalitis and AIDS
- Because of the potential immunosuppressive effects of corticosteroids, they should be discontinued as soon as clinically feasible
- Monitor closely for the development of other OIs, including cytomegalovirus (CMV) retinitis and TB disease.
- Anticonvulsants should be administered to patients with TE who have a history of seizures, but should not be administered as prophylactics to all patient

OI’s
- They continue to occur among patients for whom who we fail to initiate or reinitiate prophylaxis
- although many reports have documented longer durations of survival and shifts in the burden of disease toward more- chronic, HIV- unrelated medical conditions, OIs remain a leading cause of hospitalization and death among HIV- infected persons
Bibliography and recommended websites

- Mandell, Bennett, & Dolin: Principles and Practice of Infectious Diseases, 6th ed.
- MMWR 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) March 2009
- www.cdc.gov/mmwr
- http://hivinsite.ucsf.edu

Thank You