Pneumocystis Carinii Pneumonia (PCP) in the HAART Era

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Outline

- OIs in the HAART Era: Late Presentation
- Clinical Aspects of PCP
- PCP and the IRIS

Historical Context and Background

- PCP caused by Pneumocystis *jiroveci*, a ubiquitous organism classified as a fungus but shares biologic characteristics with protozoa.

Late Presentation in the HAART Era

HIV Highlights From Seattle
clinicaloptions.com/hiv

Patients Starting ART at Higher CD4+ Cell Counts Overall, but Disparities Remain

- CD4+ cell count at start of ART (cells/mm^3), 2009[1]

- In San Francisco study, overall trends of starting ART at higher CD4+ counts, but pts initiating ART at CD4+ counts > 350 cells/mm^3 significantly more likely to be white, older, MSM, nonpoor, and diagnosed by private provider[2]

1. Mugglin C, et al. CROI 2012. Abstract 100. 2. Truong HH, et al. CROI 2012. Abstract 139.

PCP Basics

- Remains a significant cause of death, which is associated with not receiving or failing to comply with HAART or PCP prophylaxis

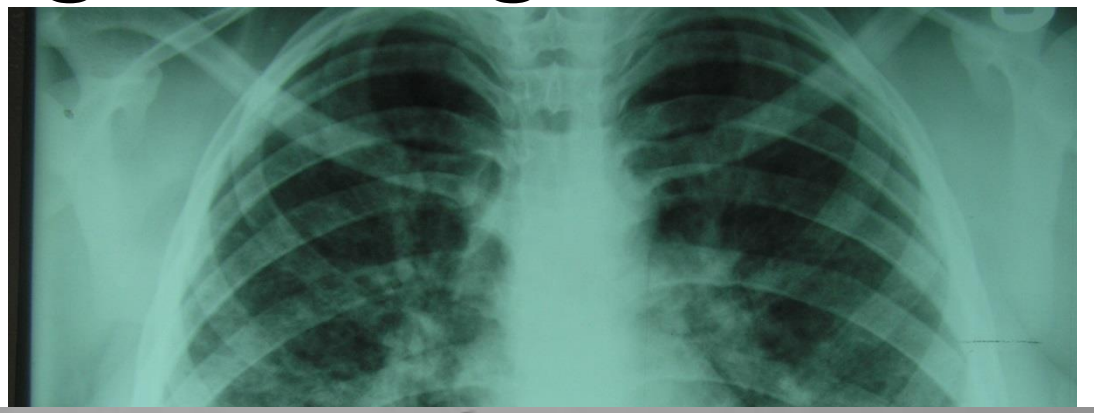
- 95% of patients who developed PCP have a CD4 count below 200 cells/mm3

Clinical manifestations:

- Generally gradual in onset
- fever (79 to 100 %)
- cough (95 %), and
- progressive dyspnea on exertion (95 %)
- Oxygenation desaturation at rest or with exercise

Radiologic findings

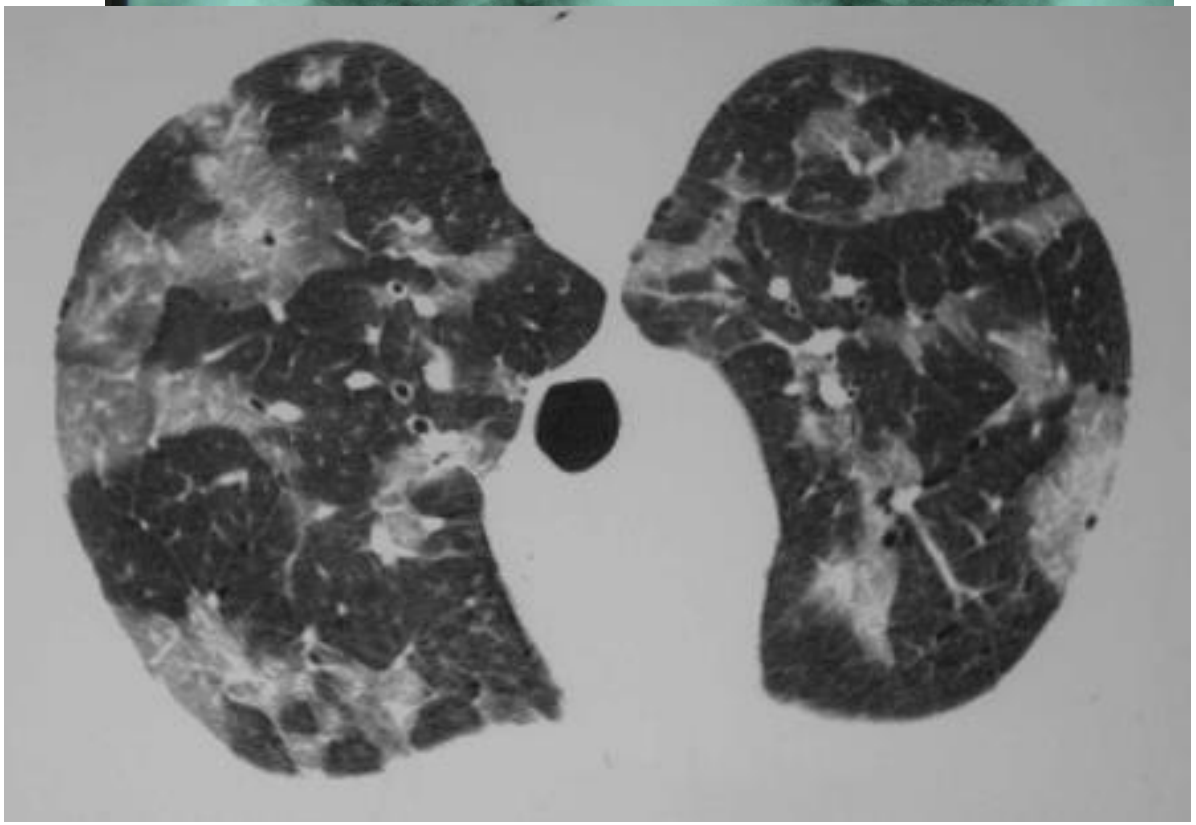
Commonly diffuse, bilateral interstitial or alveolar infiltrates (CXR or CT)



Normal CXR in 25%

at initial presentation

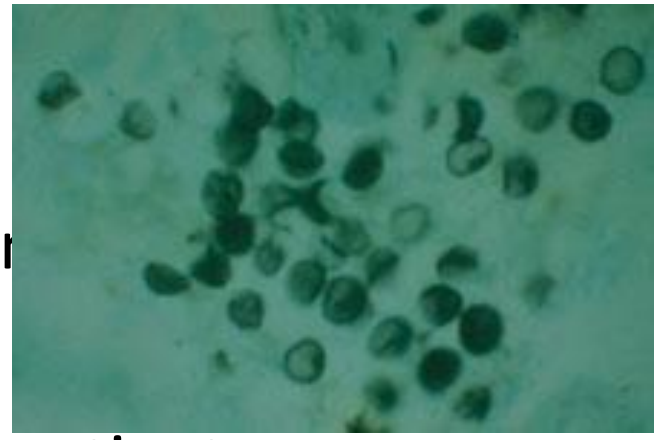
Presence of pleural effusion makes PCP unlikely diagnosis



Diagnostic Procedures

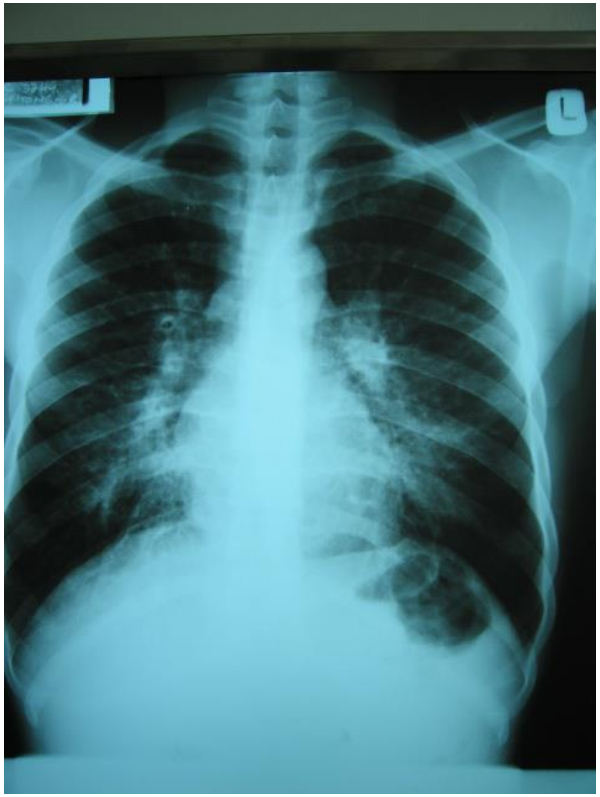
Demonstration of organisms in respiratory specimens collected by:

- Sputum induction-most rapid & least invasive. Depends on skill of lab
- Broncho-alveolar lavage - more ser
- Endoscopic aspirates-in intubated patients.
- Transthoracic needle biopsies.



PCP Differential Diagnosis

- Pulmonary TB
- Pulmonary KS
- Atypical bacterial Pneumonias



HIV-Related PCP: Treatments

	TMP/SMX	Pentamidine
Mechanism	folate antagonist DHFR inhibitor?	
Usual dose	TMP 15-20 mg/kg/d SMX 75-100mg/kg	4 mg/kg/d
Route	po, iv	iv, im
Clearance	renal	renal
Toxicities	fever, rash, hepatitis, renal failure, hypoglycemia, serum sickness, marrow hepatitis, fever, leukopenia, suppression rash, hypotension, pancreatitis	
Cure (initial Rx)	58-86%	44-99%

Alternative Antimicrobial Therapy

- Clindamycin 600-900mg iv 6-8hr + Primaquine 15-30 mg/kg base oral x 21/7
- Atovaquone 750 mg suspension bid with a meal x 21/7
- Trimetrexate +Leucovorin
- Dapsone + Trimethoprim

ADJUNCTIVE CORTICOSTEROID THERAPY FOR AIDS ASSOCIATED PNEUMOCYSTIS PNEUMONIA

- **Indications:**
- Presumed or confirmed PJP
- Moderate-severe hypoxemia
- PO_2 < 70 mm Hg (room air)
- Anti PJP therapy < 72 hours

- Regimen: *Prednisone 1mg/kg(PO) x 21 days

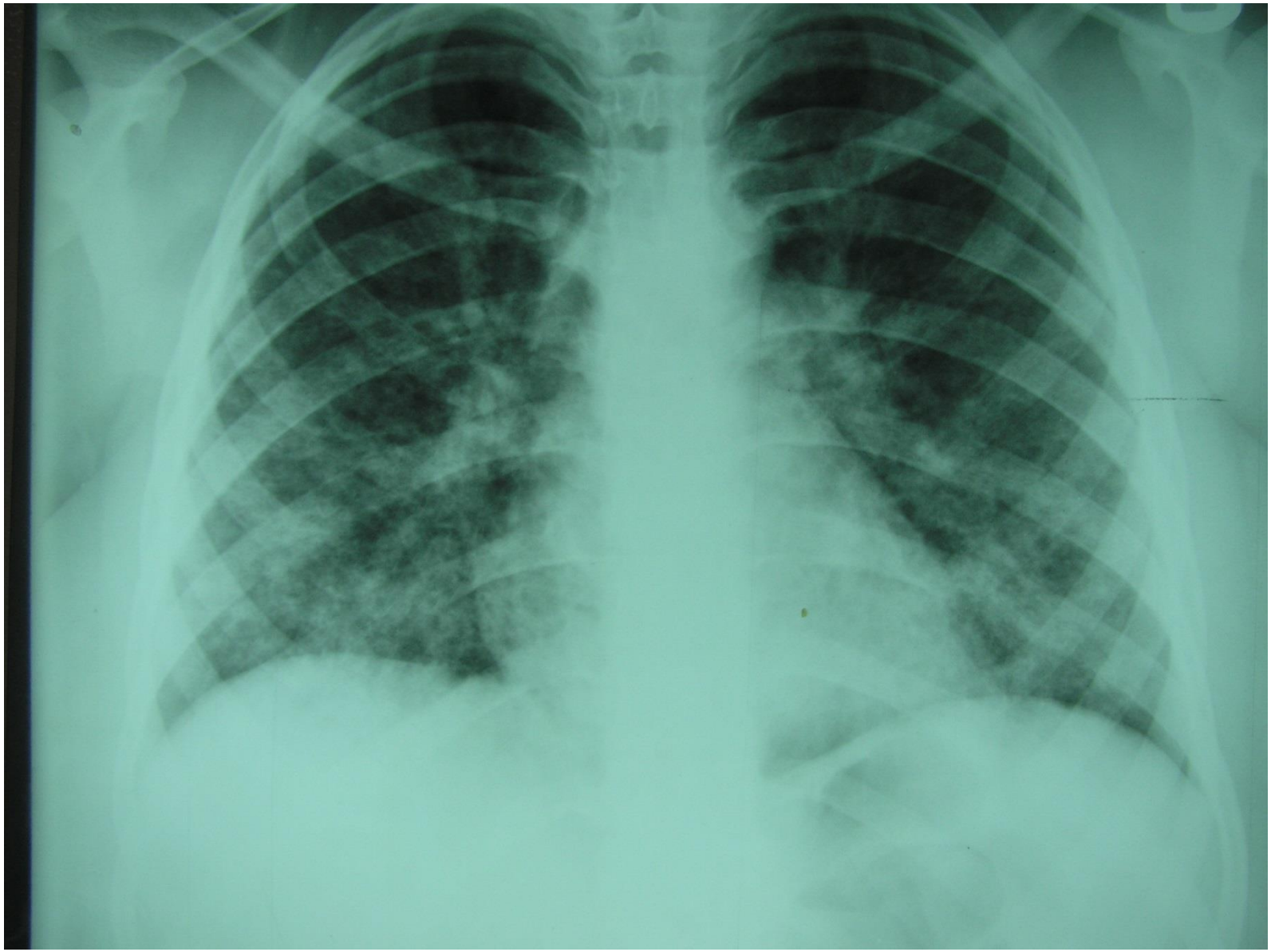
*Steroids preferably started *BEFORE* antimicrobials !!!!!!!!

Ref: Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV-infection. Briel M; Bucher H; Boscacci R; Furrer H. Cochrane Database Syst Rev. 2006 Jul 19;3:CD006150.

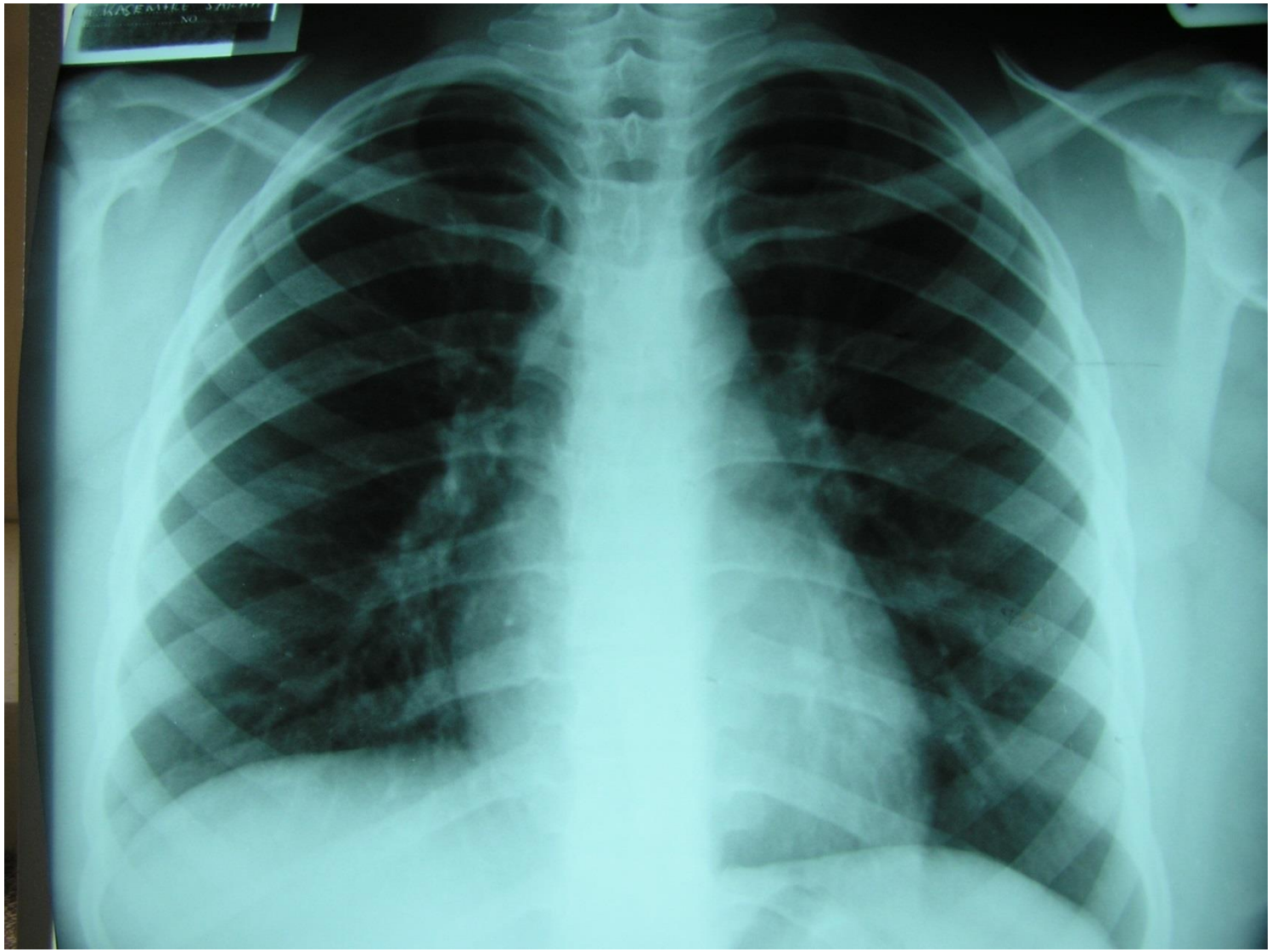
❑Use of corticosteroids

- Patients with PCP typically worsen after two to three days of therapy, presumably due to increased inflammation in response to dying organisms.
- Corticosteroids given in conjunction with anti-Pneumocystis therapy decrease the incidence of mortality and respiratory failure associated with severe PCP.
  - **~Adjunctive corticosteroids for Pneumocystis jiroveci pneumonia in patients with HIV-infection. Briel M; Bucher H; Boscacci R; Furrer H. Cochrane Database Syst Rev. 2006 Jul 19;3:CD006150.**
- **Regimen:**
  - **Dose: 1mg/kg body weight per day**
  - **21 days**

Typical Radiological Findings



Radiological Improvement can be drastic!



Prophylaxis

- Risk of PCP recurrence without prophylaxis is 60%-70% per year
- Risk is 40%-50% per year for those with CD4 <100
- PCP prophylaxis reduces the risk of PCP by 9-fold
- Patients who get PCP despite prophylaxis have a lower mortality rate

PCP and IRIS

- ACTG 5164 showed that HIV-infected patients recently diagnosed with an OI benefit from early ART (2wks compared to 8 wks).

- Pulmonary IRIS in PCP Case One case report of patient with high CD4 count[1]

- 3 cases of life-threatening PCP in a setting of early ART (Day 13, Day 23 and Day 4)[2]
  - IRIS episode occurred after completion of PCP therapy and following clinical improvement.
  - There is a need for further studies to identify risk factors of those patients who are likely to devlop life-threatening IRIS

- One case of life-threatening IRIS in a PCP patient 3 days after initiation ART, plus review of case series and case reports (n=32)[3]
  - Time to PCP IRIS varied widely (3-301 days. All cases associated with brisk viral load reduction

1-Mori S, Polatino S, Estrada-Y-Martin RM.. Int J STD AIDS. 2009 Sep;20(9):662-5.
2-Jagannathan P, Davis E, Jacobson M, Huang L. AIDS. 2009 Aug 24;23(13):1794-6
3-Mok HP, Hart E, Venkatesan P Int J STD AIDS. 2014 Apr;25(5):373-7.

Acknowledgements

- IDI Clinic Archive

- Clinical Care Options HIV