Pneumocystis Pneumonia: Prevention & Treatment

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Pneumocystis Pneumonia

- Prevention
  - Criteria for starting & stopping prophylaxis
  - Prophylaxis options & other considerations
- Treatment
  - Recommended agents for mild-moderate or severe PCP/PJP
  - Adjunctive therapy & managing non-response to treatment

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Review

What kind of organism is *Pneumocystis*?

A) Bacteria

B) Virus

C) Protozoa

D) Fungus

Review

What is unique about *Pneumocystis* compared to other fungi?

A) Cell wall contains a polysaccharide component called galactomannan

B) Lacks common fungal cell wall components (e.g., ergosterol)

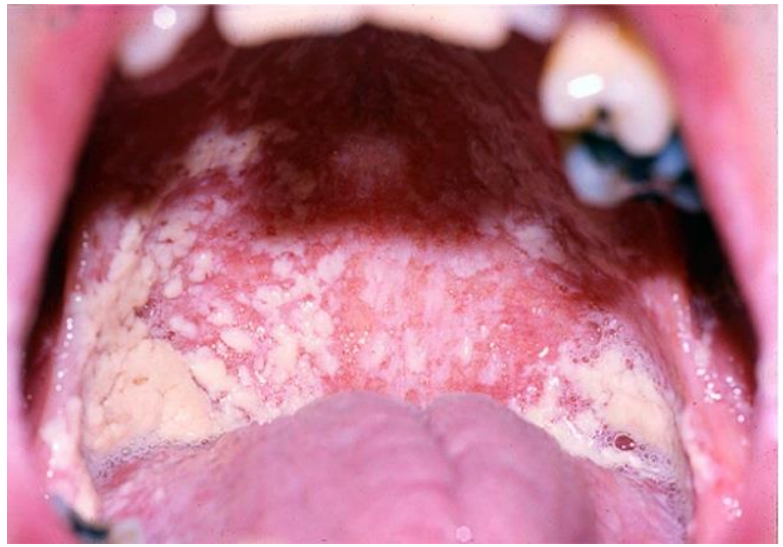
C) Grows as broad hyphae with right-angle branching visible on culture

D) Dimorphic (can exist as mold or yeast depending on temperature)

Pneumocystis: Prevention

Pneumocystis Prevention
Initiating Primary Prophylaxis for Adults & Adolescents, Including Pregnant Persons

- Indications:
  - **CD4 count <200 cells/mm^3 (AI)**
  - CD4 percentage <14% (BII)
  - CD4 count 200-250 cells/mm^3, not taking ART, and can't monitor frequently (BII)
  - Oral thrush or AIDS-defining illness (speaker addition)



OI Guidelines (clinicalinfo.hiv.gov)
Image from: National HIV Curriculum (hiv.uw.edu)

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Pneumocystis Prevention
Options for Prophylaxis

Trimethoprim-sulfamethoxazole	• DS tab daily preferred; also prevents toxoplasmosis (AI) • SS tab daily effective & may be better tolerated (AI) • DS tab 3 times per week also effective (BI)
Dapsone	• Check G6PD level • 100 mg daily (BI); does not prevent toxoplasmosis
Atovaquone	• Liquid, expensive • 1500 mg daily (BI); may prevent toxoplasmosis
Inhaled pentamidine	• Several limitations • 300 mg monthly (BI); does not prevent toxoplasmosis

OI Guidelines (clinicalinfo.hiv.gov)

Pneumocystis Prevention
Discontinuing Prophylaxis

- **CD4 count >200 cells/mm^3 for at least 3 months (AI)**
- European COHERE database review (>23k PWH, >100k PYFU)
  - CD4 101-200 cells/mm^3 and HIV RNA <400 copies/mL
    - No difference in PCP incidence if receiving primary prophylaxis or not
    - 0 cases of PCP in those who discontinued primary prophylaxis
- "One approach…" stop prophylaxis when CD4 count 100-200 cells/mm^3 if HIV RNA below limits of detection for ≥3-6 months (BII)

OI Guidelines (clinicalinfo.hiv.gov)
COHERE: Mocroft A, et al. Clin Infect Dis. 2010;51(5):611-9.

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Pneumocystis Prevention
Preventing Exposure & Isolation of Hospitalized Patients

- Preventing initial exposure difficult; largely ubiquitous organism
- Should hospitalized patients with PCP/PJP be separated from other immunosuppressed hospitalized patients? Yes
  - Organism can be detected/quantified in air near patients with infection
  - Outbreaks in renal transplant and other units documented
- CDC: “avoid placement in the same room as an immunocompromised patient”

OI Guidelines (clinicalinfo.hiv.gov)
Hauser PM, et al. Clin Infect Dis. 2010;15;51(4):e28-33.
Rabodonirina M, et al. Emerg Infect Dis. 2004;10:1766-73
CDC: https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html

Pneumocystis: Treatment

Pneumocystis Treatment
Recommended Options

-Outpatient
-No significant hypoxia
-Able to take PO
-Adherent to meds

Mild disease

- **Oral TMP-SMX (AI)**
- TMP + Dapsone* (BI)
- Clindamycin + Primaquine* (BI)
- Atovaquone (BI)

Severe disease

- **IV TMP-SMX (AI)**
- IV Pentamidine (AI)
- Clindamycin + Primaquine* (AI)

-Inpatient
-Significant hypoxia
-Unable to take PO
-Comorbidities
-Remember illness may worsen initially!

- RCT's all done prior to 1999
- TMP-SMX dose based on limited data
- Patient population, ART use, and critical care protocols different
- Retrospective data: lower TMP-SMX doses as effective, better tolerated
- OI guidelines: lower doses may be considered, but RCT data unavailable

- TMP-SMX dosing study: RCT planned (NCT04851015) comparing 10 mg/kg/day TMP vs 15 mg/kg/day
- McDonald et al: consider lower dose if older, baseline CKD, hyperK, low suspicion for PCP/PJP

*Check G6PD

OI Guidelines (clinicalinfo.hiv.gov)
McDonald EG, et al. OFID 2021.
Tritle BJ, et al. Transplant Infect Dis 2021.
Butler-Laporte G, et al. OFID 2020.
Thomas M, et al. Scand J Infect Dis 2009.

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Pneumocystis Treatment
Key Clinical Reminders

- Empiric treatment ok? **Yes**
- Standard course: **21 days**
- Corticosteroids if: **PaO2 <70 or A-a gradient ≥35** (ABG is key!)
  - Oral prednisone (start ASAP, ideally within 72 hours of initiating treatment)
    - Example: days 1–5: 40 mg BID, days 6–10: 40 mg QD, days 11–21: 20 mg QD
  - Or, IV methylprednisolone at 75% of prednisone doses
- Alter treatment based on prophylaxis? **No**
- Start ART within 2 weeks of PCP treatment? **Yes**

Huang L, et al. Proc Am Thorac Soc. 2011;8(3):294-300.
OI Guidelines (clinicalinfo.hiv.gov)

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Pneumocystis Treatment
Considering Treatment Non-Response

- Illness often worsens during first **3 to 5 days**
  - Wait **4 to 8 days** before switching therapy for lack of clinical improvement
- What to do if suspect treatment failure? Unclear…
  - Rule out concomitant infection (e.g., obtain or repeat BAL)
  - Switch oral meds to IV? IV med to alternate agent?
  - Add additional agent? Add echinocandin?
  - Increase steroid dose? Prolong the steroid taper?
  - Extend treatment (and steroid) duration?

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