NORTHWEST AIDS EDUCATION AND TRAINING CENTER

Pneumocystis Pneumonia (PCP): Part 2

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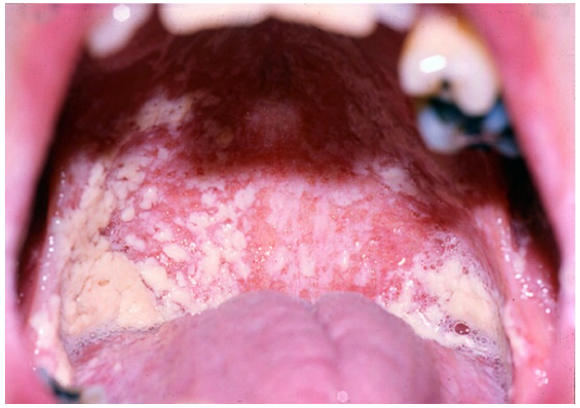
Pneumocystis Pneumonia (PCP): Part 2

- Prevention
  - Initiating Prophylaxis
  - Discontinuing Prophylaxis
  - Other Considerations
- Treatment
  - Recommended Agents
  - Managing Side Effects/Treatment Failure
  - Drug Resistance

Prevention

Initiating Prophylaxis

- Indications for prophylaxis:
  - **CD4 count <200 cells/mm^3 (AI)**
  - **Oral thrush (AII)**
  - CD4% <14 or other AIDS-defining illness (BII)
  - Following PCP treatment (secondary prophylaxis)



Kaplan JE, Benson C, Holmes KK et al. CDC MWR 2009;58(RR-4):1-207.

Options for Prophylaxis

Trimethoprim-Sulfamethoxazole (TMP-SMX)	• DS or SS tab daily recommended (AI) • DS tab 3x/week an alternative (BI)
Dapsone	• Check G6PD level • 100 mg daily
Atovaquone	• Liquid, expensive • 1500 mg daily
Inhaled Pentamidine	• Several limitations • 300 mg monthly

Kaplan JE, Benson C, Holmes KK et al. CDC MWR 2009;58(RR-4):1-207.

Discontinuation of Prophylaxis

- **CD4 count >200 cells/mm^3 for at least 3 months**
- Systematic review of early discontinuation:
  - CD4 <200 cells/mm^3 and suppressed viral load
  - Overall rate of PCP: 0.48/100 person-years
  - Inadequate data for CD4 ≤100

1) Kaplan JE, Benson C, Holmes KK et al. CDC MWR 2009;58(RR-4):1-207.
2) Costinuik CT, Fergusson DA, Doucette S, Angel JB. PLoS One 2011;6(12): doi: 10.1371/journal.pone.0028570

Early Discontinuation of Prophylaxis

Study	Site	Type	# Subjects	Criteria	PCP Rate
Soriano et al (AIDS 2000)	Madrid, Spain	Retrospective	29 (secondary prophylaxis only)	VL <500 after 3 months ART	1/522 patient months
D'Egidio et al (AIDS 2007)	Ottawa, Canada	Prospective	19	VL <50 for ≥3 months	0/261 patient months
COHERE (CID 2010)	**29 European cities**	**Prospective**	**23,412 (primary prophylaxis only)**	**VL <400**	**0/1000 patient years**
Cheng et al (BMC ID 2010)	Thailand	Retrospective	215	VL <400	0.31/100 patient years

Prevention of Exposure

- Difficult because ubiquitous organism
- Should infected hospitalized patients be isolated?

  1) Study in France and Switzerland:
    - % with DHPS mutation who had never been exposed to sulfa: 29.7% in Lyon, France vs. 3% in Switzerland
    - Lyon did not have policy of isolating/separating PCP patients

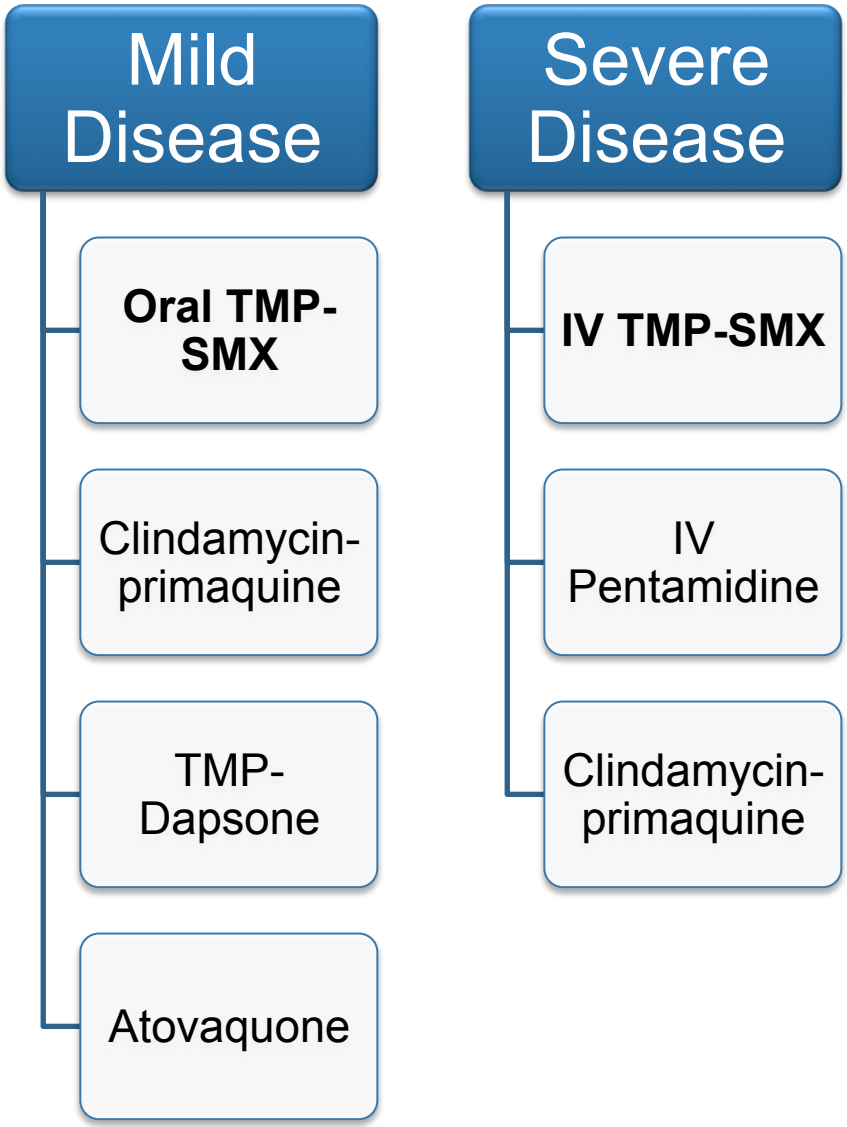
  2) Outbreak among renal transplant recipients

1) Hauser PM, et al. Clin Infect Dis 2010;15;51(4):e28-33. doi: 10.1086/655145
2) Rabodonirina M et al. Emerg Infect Dis 2004;10:1766-73

Treatment

Treatment Options

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



-Inpatient
-Significant hypoxia
-Unable to take PO
-Comorbidities
-Need pentamidine

Key Treatment Considerations

- Empiric treatment ok? **Yes**
- Standard course: **21 days**
- Corticosteroids if: **PaO2 <70 or A-a gradient >35**
- Pregnancy: **TMP-SMX**
- Treatment based on prophylaxis? **No**

Huang L et al. HIV-Associated Pneumocystis Pneumonia. Proc Am Thorac Soc 2011;8(3): 294-300.

Managing Side Effects

TMP-SMX	*Dapsone	Atovaquone	Clindamycin	*Primaquine	Pentamidine
Rash	Rash	Rash	Rash	Agranulo-cytosis	Electrolyte changes
Renal/ hepatic dysfunction	Hemolytic anemia	Hepatic dysfunction	C. diff	Hemolytic anemia	Renal / hepatic dysfunction
HyperK	Cytopenias	GI symptoms	GI symptoms	Cytopenias	Arrhythmias
GI symptoms	Methemo-globinemia				Hypotension
Cytopenias					Hypoglycemia
					Pancreatitis
					Cytopenias

*Remember to check G6PD level

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Treatment Failure

- May worsen in first **2-3** days but should improve by days **5-7**; if not, consider the following:
  - Rule out concomitant infection
  - Switch oral meds to IV? IV med to alternate agent?
  - Add additional agent?
  - Increase steroid dose?
  - Extend duration?
  - Add an echinocandin?

Prognosis

- Factors associated with poor outcome in PCP:
  - **Severe disease**:
    - Hypoxia, ICU admission, mechanical ventilation
  - **Advanced immunosuppression**
  - Older age
  - Higher LDH
  - Prior episodes of PCP
  - Low albumin

Antinori A et al. Eur J Epidemiol. 1993;9(2):183.

Drug Resistance

- DHFR gene mutation (from TMP)
- DHPS gene mutation (from SMX or dapsone)
  - More Common
- Some association with treatment failure, not always
  - Other factors likely more important
- Bottom line: **TMP-SMX** always first line

Huang L et al. HIV-Associated Pneumocystis Pneumonia. Proc Am Thorac Soc 2011;8(3): 294-300.

Summary

- Prophylaxis indicated if CD4 <200, thrush, prior PCP
- Stop if CD4 >200 for 3 months, though likely safe if CD4 100-200 and VL undetectable
- Should likely separate patients with PCP from other immunosuppressed patients
- First-line for prophylaxis and treatment: TMP-SMX
- Many possible drug side effects and no clear guidelines for managing treatment failure