

Pneumocystis Pneumonia: Treatment

Aley Kalapila, MD, PhD

Associate Editor, National HIV Curriculum

Associate Professor of Medicine

Division of Infectious Diseases

Emory University School of Medicine & Grady Health System

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Pneumocystis pneumonia (PCP) Treatment: Outline

- Background
- Clinical Manifestations & Diagnosis
- Treatment
- Medication side effects
- Summary

Background

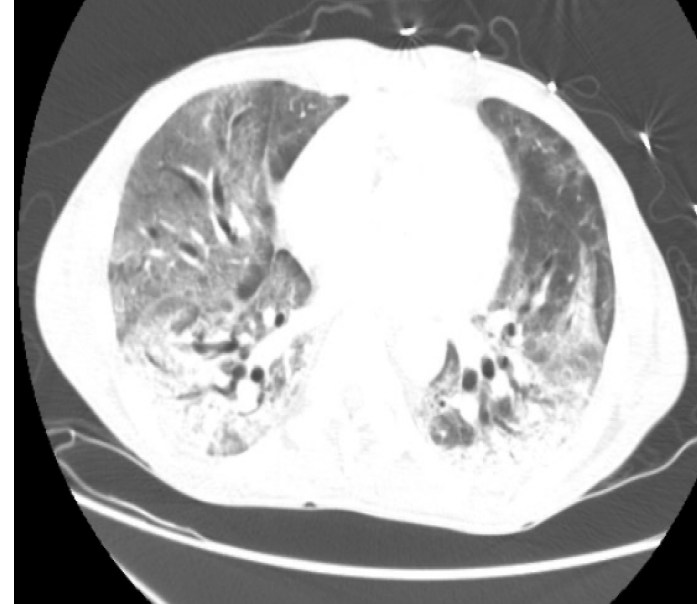
Background - *Pneumocystis* Pneumonia

- Major cause of pneumonia in PWH when CD4 count <200 cells/mm³
- Caused by the ubiquitous fungus, *Pneumocystis jirovecii*
- Airborne transmission
- Disease occurs by new acquisition vs reactivation of latent infection
- Symptoms include fever, hypoxia, dyspnea, non-productive cough
- Rates of disease have decreased with wider use of ART and TMP-SMX for prophylaxis

Clinical Manifestations & Diagnosis

Clinical Manifestations

- Common symptoms include subacute dry cough, progressive dyspnea on exertion, fever and hypoxemia
- With worsening disease severity, chest x-ray (CXR) usually shows diffuse bilateral infiltrates
- High-resolution CT scan of chest is more sensitive than (CXR). CT findings may include:
 - Interstitial abnormalities including ground glass opacities
 - Pneumatoceles
 - Cystic lesions
 - Pneumothoraces



Chest CT

Diagnosis of *Pneumocystis* Pneumonia

- Presumptive diagnosis is made based on presentation, symptoms, chest imaging, oxygen desaturation, high lactate dehydrogenase (LDH) and 1,3-beta-D-glucan level
- Definitive diagnosis requires histopathologic or cytopathologic identification of the organism on induced sputum, BAL or tissue using either:
 - Direct immunofluorescence stain OR
 - PCR
- *Pneumocystis* PCR testing is highly sensitive and does not distinguish between active infection and colonization
- PCP Treatment can be initiated presumptively while awaiting definitive diagnostics

Treatment

Treatment of Mild to Moderate *Pneumocystis* Pneumonia

Treatment Duration = 21 days

PREFERRED REGIMEN	ALTERNATIVE REGIMENS
TMP-SMX PO	Dapsone PO ^a + TMP PO <i>or</i> Primaquine PO ^a + Clindamycin PO <i>or</i> Atovaquone PO

NOTES:

^a Check G6PD levels prior to using dapsone or primaquine

Moderate to Severe *Pneumocystis* Pneumonia: Case Definition

- Room air PO₂ < 70mm Hg
- Alveolar – arterial O₂ gradient ≥35 mm Hg

Treatment of Moderate to Severe *Pneumocystis* Pneumonia

Treatment Duration = 21 days

PREFERRED REGIMEN

TMP-SMX IV at the start of treatment

Can switch to PO TMP-SMX with clinical improvement

ALTERNATIVE REGIMENS

Primaquine PO + Clindamycin (IV or PO) *or* Pentamidine IV

Check G6PD levels prior to using primaquine

Adjunctive corticosteroids should be initiated as soon as possible (ideally within 72h) for moderate to severe PCP

- Oral Prednisone or IV methylprednisolone tapered over 21 days

Treatment Failure

- Defined as lack of improvement or worsening respiratory function (with arterial blood gas) after 4-8 days of PCP treatment initiation
 - Wait 4-8 days before switching therapy
 - Evaluate for concomitant infections, ideally by using bronchoscopy with BAL
- Treatment failure due to treatment limiting toxicities may occur
 - Switch to another regimen
 - Prior studies suggest that clindamycin and primaquine combination may be more effective salvage regimen

After PCP Treatment completion

- Resume prophylaxis until CD4 cell count ≥ 200 cells/mm³ for at least 3 months after ART initiation
 - Can consider discontinuing secondary prophylaxis if CD4 cell count is 100-200 cells/mm³ and undetectable HIV RNA for ≥ 3 months
- Initiate ART within 2 weeks of PCP diagnosis
- IRIS is rare

Side Effects of Medications Used for PCP Treatment

Potential Side Effects of Medications Used for PCP Treatment

Medication	Potential Side Effects
TMP-SMX	Renal dysfunction, hyperkalemia, leukopenia, rash, hepatitis
Dapsone*	Hemolytic anemia (if used in patients with G6PD deficiency)
IV Pentamidine	Injection site reaction, renal dysfunction, hypotension, confusion, hypoglycemia, hepatitis, leukopenia
Atovaquone	Bad taste
Clindamycin	Diarrhea
Primaquine	Hemolytic anemia (if used in patients with G6PD deficiency), prolonged QTc, arrhythmias, rash, GI symptoms

*Contains sulfonamide and there is potential for cross-reactivity with other sulfa-containing drugs; dapsone not contraindicated in patients with sulfonamide allergy

Summary

PCP Treatment: Editor's Summary

- *Pneumocystis jiroveci* is a major cause of pneumonia in PWH with a CD4 <math><200\text{ cells/mm}^3</math>
- PCP treatment can be initiated presumptively based on presentation and imaging, while awaiting definitive diagnosis
- Definitive diagnosis requires identification of organism on respiratory specimens
- The preferred drug for PCP treatment is TMP-SMX
- Adjunctive corticosteroids are indicated for moderate to severe PCP
- ART can be initiated within 2 weeks of PCP diagnosis

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