Pneumocystis Pneumonia: Part 1

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No conflicts of interest or relationships to disclose.
Pneumocystis Pneumonia: Part 1

• Background & biology
• Clinical manifestations
• Diagnosis
Pneumocystis: Background & Biology
Pneumocystis: Background

• Identified 1909 by Chagas; reported as part of life cycle of *Trypanosoma cruzi*
• Recognized as separate organism in 1912; named *Pneumocystis carinii*
• 1940s-50s: pneumonia epidemics in premature and malnourished infants
• 1980s-90s: leading cause of death in individuals with advanced HIV
Pneumocystis: Biology

- Initially classified as protozoa; now an atypical **fungus**
  - Lacks many typical fungal cell wall components (e.g., ergosterol)
  - Can’t be cultured
- Each mammalian species infected with unique strain
  - *Pneumocystis carinii*: rats
  - *Pneumocystis jirovecii*: humans
- Worldwide, near ubiquitous exposure: most exposed in infancy
Pneumocystis Disease: Reactivation vs New Infection

**Reactivation**
- Most colonized by infancy
- Disease in animals if immunosuppress

**New Infection**
- Animals develop infection when exposed
- Repeat infection different strains
- Clusters of cases with same genotype

Pneumocystis: Risk Factors

- **Key = Immunosuppression**
  - Multicenter AIDS Cohort Study:
    - Incidence with CD4 count 201 to 350 = 0.5%
    - Within 6 months of falling below 200 = 8.4%
    - Within 12 months of falling below 200 = 18.4%
    - Within 6 months of developing thrush = 29.5%
  - Key risk factors: CD4 <200, CD4% <14%, oral thrush, previous PCP

- Environmental factors?

- Exposure to infected or colonized persons?

Pneumocystis: Clinical Manifestations
## Pneumocystis: Clinical Manifestations

<table>
<thead>
<tr>
<th>Symptoms</th>
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<tbody>
<tr>
<td>Fever, chills, fatigue, malaise</td>
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<td>Dyspnea (“door-stop”)</td>
</tr>
<tr>
<td>Dry cough</td>
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<tr>
<td>Pleuritic chest pain</td>
</tr>
<tr>
<td>*<strong>Usually subacute (mean 3 weeks)</strong></td>
</tr>
</tbody>
</table>

- **Symptoms**: Fever, chills, fatigue, malaise; Dyspnea (“door-stop”); Dry cough; Pleuritic chest pain.
- **Signs**: Hypoxia (especially with exertion); Diffuse, bilateral, interstitial infiltrates; Ground glass opacities, sometimes mosaic or geographic pattern; Dyspnea (“door-stop”); Tachypnea, tachycardia; Pneumothorax; Septal thickening, “crazy paving”.
- **Chest X-Ray**: Dry cough; Inspiratory crackles; Pleural effusion, lobar infiltrate, nodules less common; Thin-walled cystic lesions.
- **Chest CT**: Pneumothorax; Septal thickening, “crazy paving”.
- **Symptoms usually subacute (mean 3 weeks)**
- **Chest Exam**: Normal in 50%
- **Chest X-Ray**: Normal in 25%
- **High-Resolution CT**: Usually abnormal.
Pneumocystis: Diagnosis
Pneumocystis: Diagnosis

• **Gold standard**: identification of organism on stain of respiratory secretions or tissue; organism has never been reliably cultured
  - Chemical stain (methenamine silver, toluidine blue, calcofluor white)
  - Immunofluorescence (IF) stain (*preferred*)

• Induced sputum: sensitivity <50-90%
  - Generally not improved by repeating

• Bronchoscopy with BAL: sensitivity 90-99%

• Lung biopsy: sensitivity 95-100%

2) CDC OI Guidelines. PCP section last updated March 2019. clinicalinfo.hiv.gov
Image of cysts on IF stain from CDC (https://www.cdc.gov/dpdx/pneumocystis/index.html)
Pneumocystis Diagnosis: Respiratory Specimen PCR

• Higher sensitivity than staining methods
• Specificity is an issue: infection versus colonization?
  • Detects organism in many asymptomatic & immunocompetent persons
• Quantitative better than qualitative, but cutoffs used in literature variable
• Correlate with clinical/radiologic findings!

Table 2. Diagnostic Criteria for Definition of Proven and Probable Pneumocystis jirovecii Pneumonia

<table>
<thead>
<tr>
<th>Description</th>
<th>Proven PCP</th>
<th>Probable PCP</th>
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<tbody>
<tr>
<td>- Clinical and radiologic criteria, plus:</td>
<td>- Demonstration of <em>P. jirovecii</em> by microscopy using conventional or immunofluorescence staining in tissue or</td>
<td>- Appropriate host factors and clinical and radiologic criteria, plus:</td>
</tr>
<tr>
<td>- Demonstration of <em>P. jirovecii</em> by microscopy using conventional or immunofluorescence staining in respiratory specimens</td>
<td></td>
<td>- Amplification of <em>P. jirovecii</em> DNA by quantitative real-time PCR in respiratory specimen or</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Detection of β-D-glucan in serum (alternative method; another IFD and a false-positive result should be ruled out)</td>
</tr>
</tbody>
</table>

Abbreviations: IFD, invasive fungal diseases; PCP, *Pneumocystis jirovecii* pneumonia; PCR, polymerase chain reaction.

Pneumocystis Diagnosis: Blood Tests

- **LDH:**
  - Non-specific; prognostic?

- **1-3-Beta-D-Glucan:**
  - Sensitivity 93%, specificity 75%
  - May be elevated in some other invasive fungal infections (eg, histo)

<table>
<thead>
<tr>
<th>1-3-Beta-D-Glucan Characteristics</th>
<th>High Pre-Test Probability</th>
<th>Low Pre-Test Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-test probability of negative result</td>
<td>40%</td>
<td>8%</td>
</tr>
<tr>
<td>Post-test probability of positive result</td>
<td>96%</td>
<td>57%</td>
</tr>
</tbody>
</table>

1) Gilroy SA, Bennett NJ. Semin Respir Crit Care Med 2011;32(6):775-82.
Pneumocystis: Summary of Diagnostic Pathway

- CXR; if normal and high suspicion → high-resolution chest CT
- Blood tests: ABG, beta-D-glucan (if available), +/- LDH
- Induced sputum: IF stain (or PCR)
- If induced sputum negative → bronchoscopy/BAL IF stain (or PCR)
- Lung biopsy if still unclear (rarely needed)
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