

Pneumocystis Pneumonia: Part 1

Brian R. Wood, MD

Medical Director, MWAETC Project ECHO

Associate Professor of Medicine, University of Washington

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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

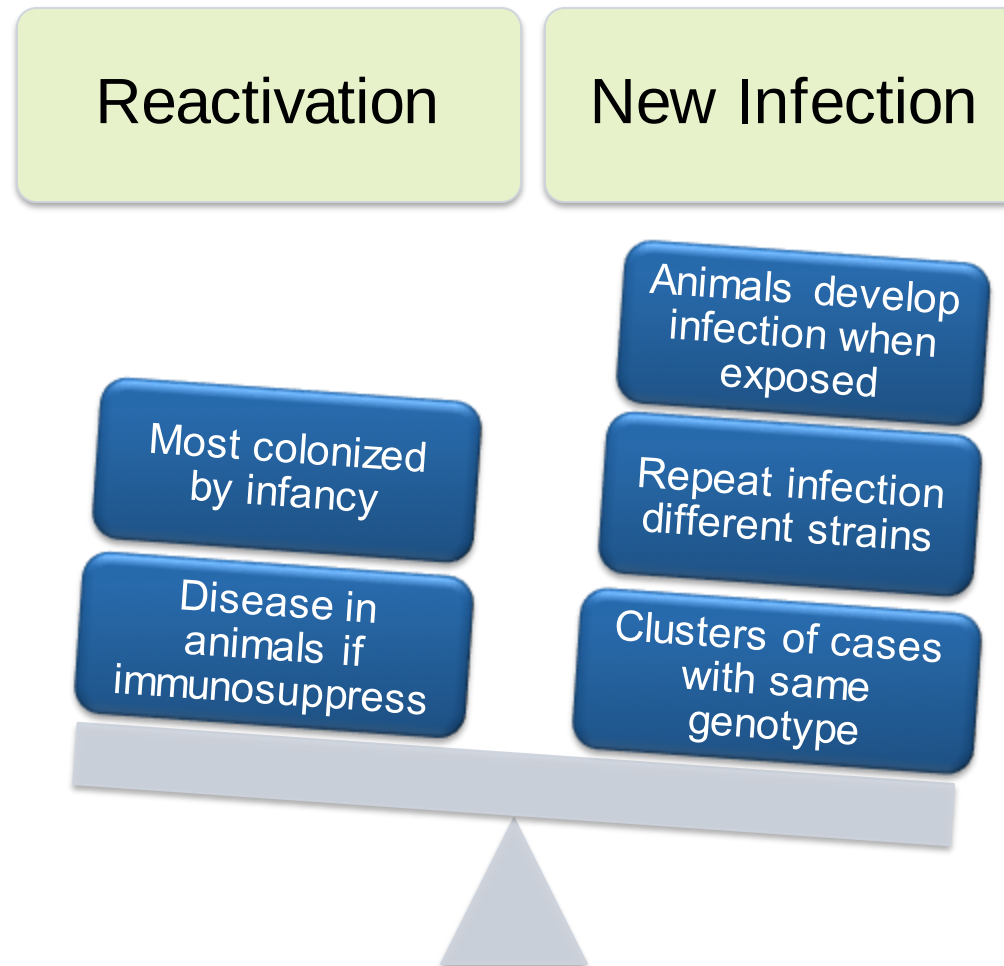
- Identified 1909 by Chagas; reported as part of life cycle of *Trypanosoma cruzi*
- Recognized as separate organism in 1912; named *Pneumocystis carinii*
- 1940s-50s: pneumonia epidemics in premature and malnourished infants
- 1980s-90s: leading cause of death in individuals with advanced HIV

Pneumocystis: Biology

*Is it “PCP” or “PJP?”
Either is ok!*

- 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



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?

1) Phair J, et al. NEJM. 1990, 322(3): 161-165.

2) Djawe K, et al. Clin Infect Dis. 2013;56(1):74-81.

Pneumocystis: Clinical Manifestations

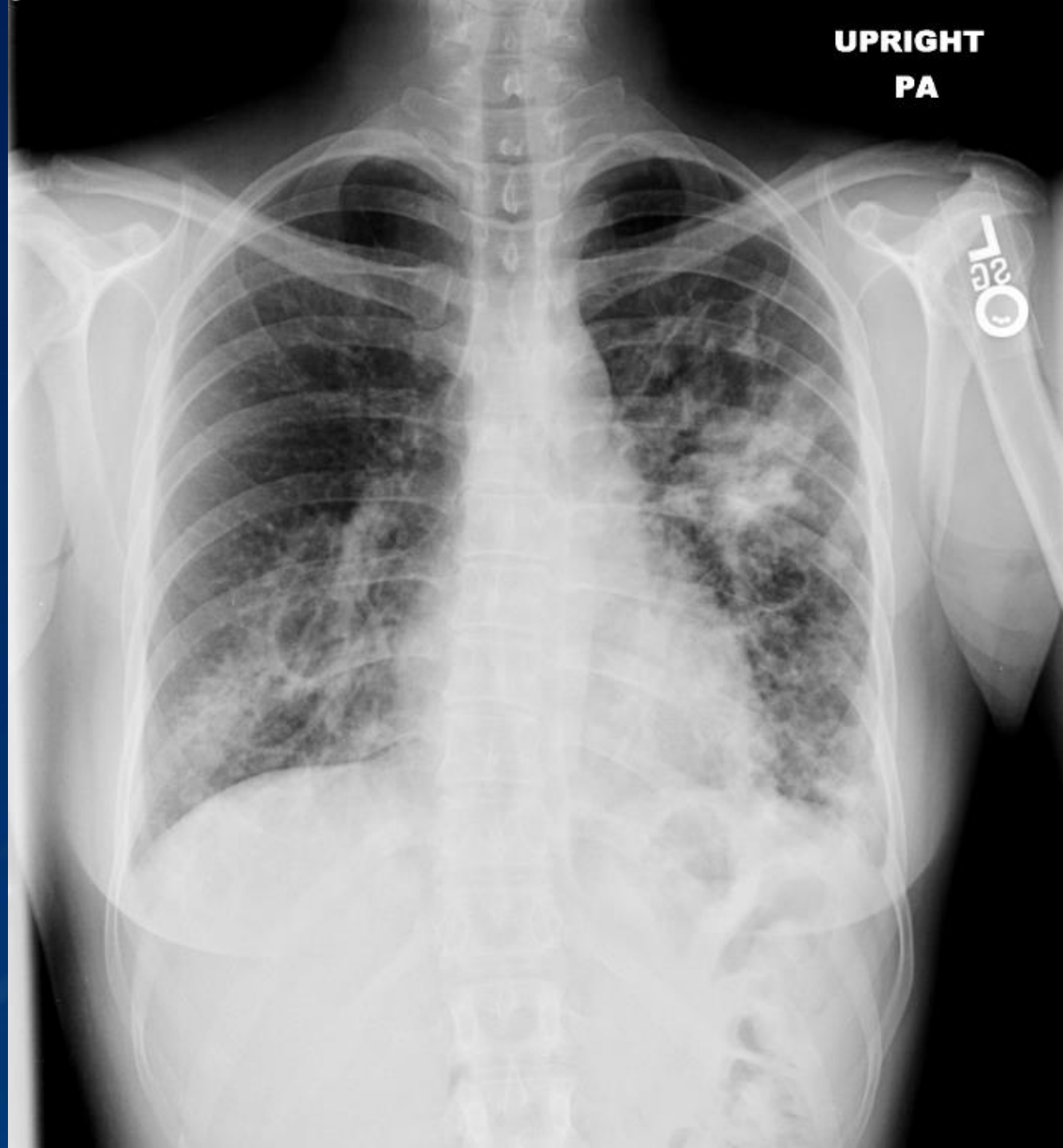
Pneumocystis: Clinical Manifestations

Symptoms
Fever, chills, fatigue, malaise
Dyspnea (“door-stop”)
Dry cough
Pleuritic chest pain
*Usually subacute (mean 3 weeks)

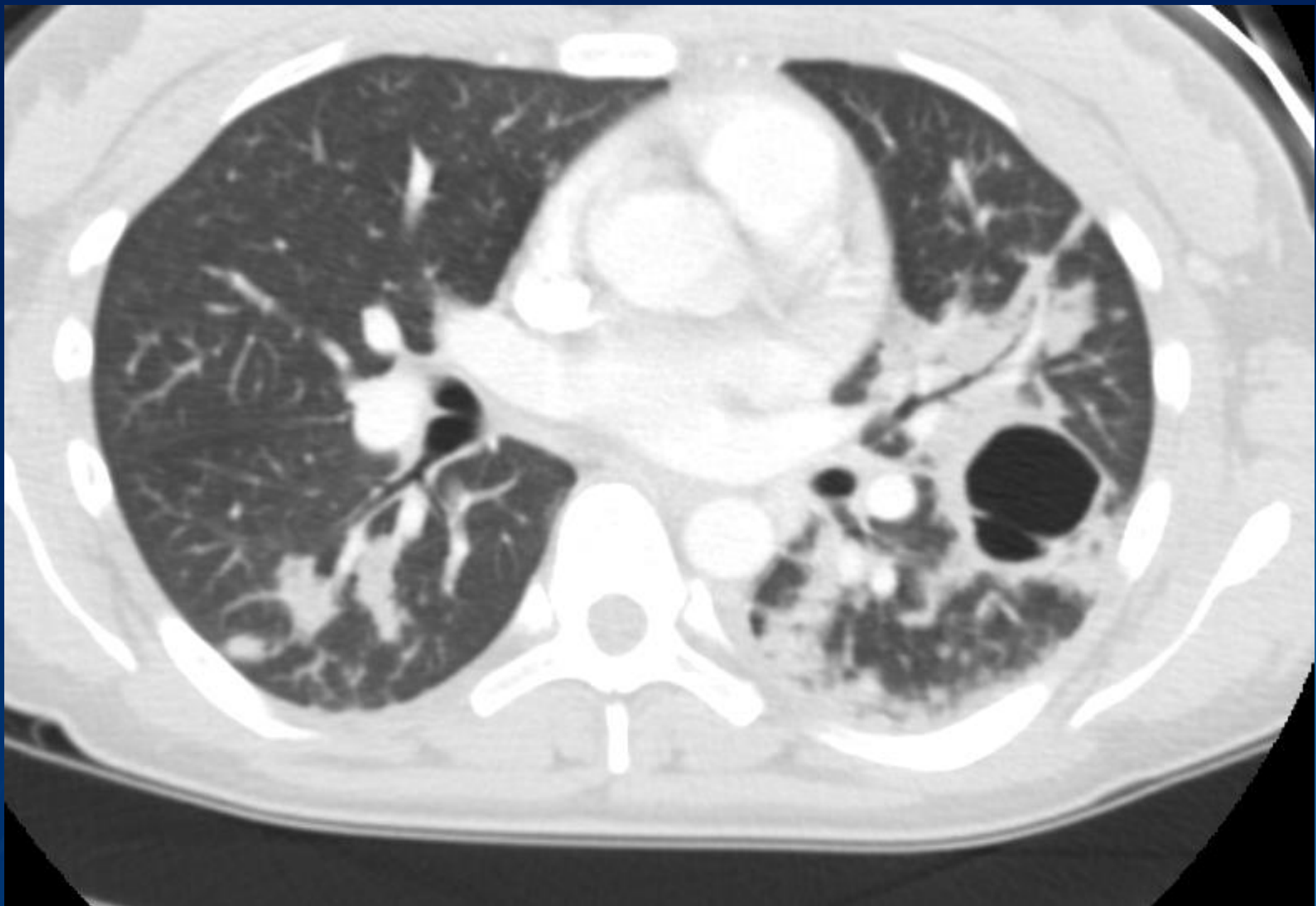




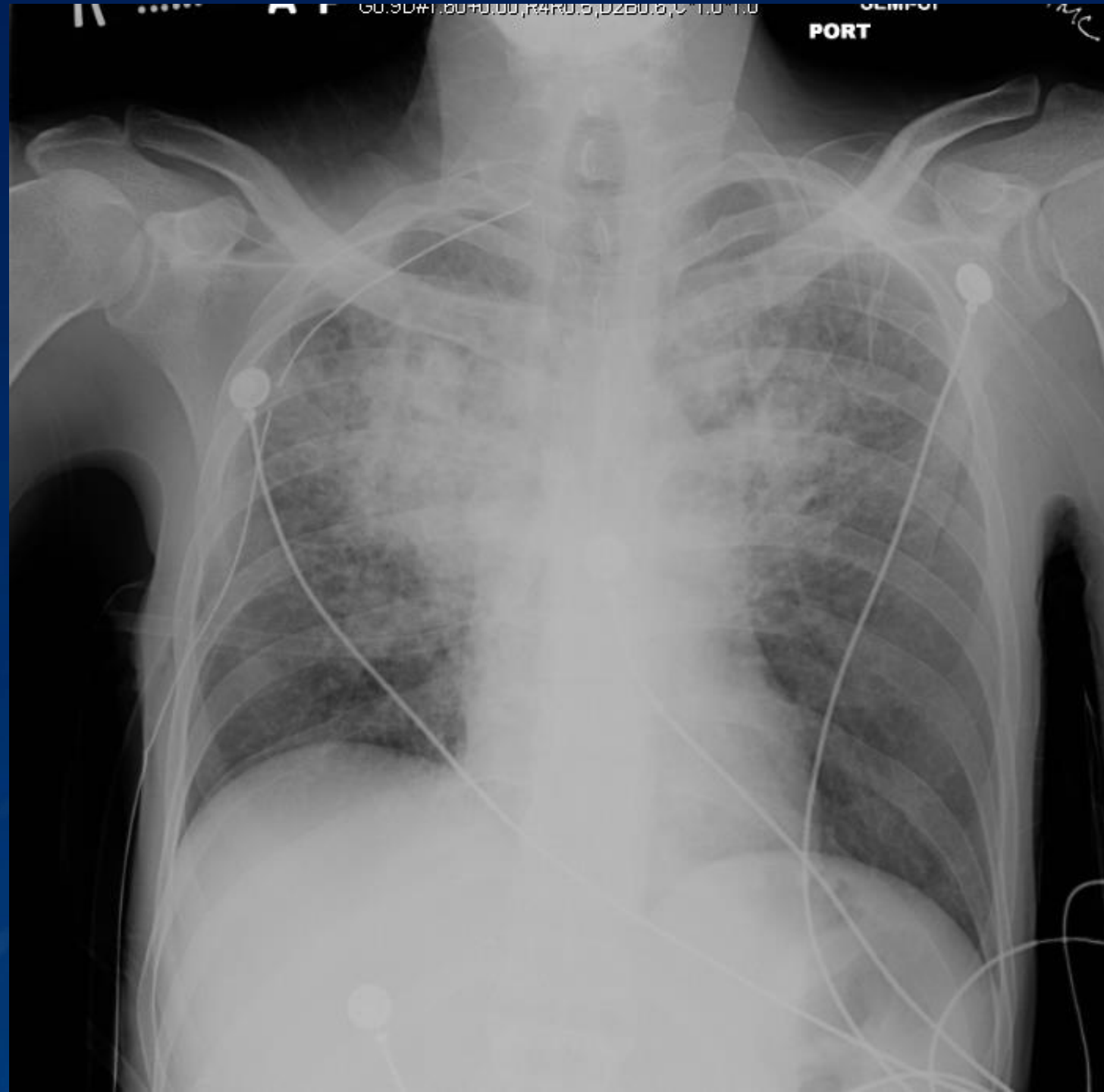
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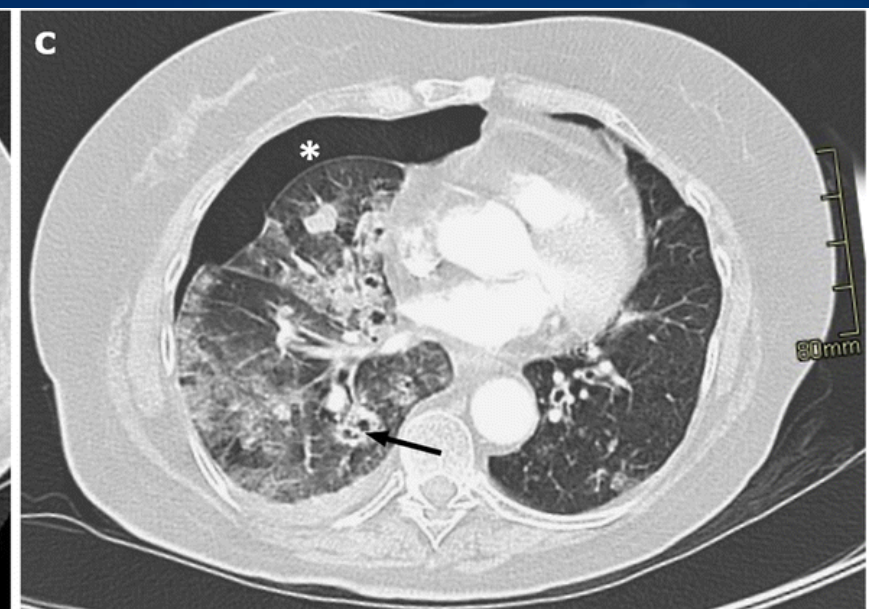
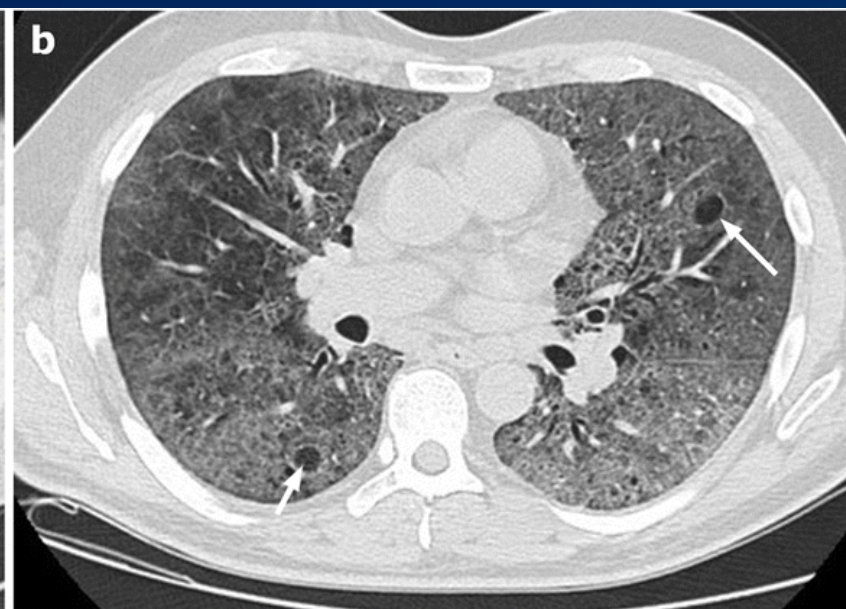
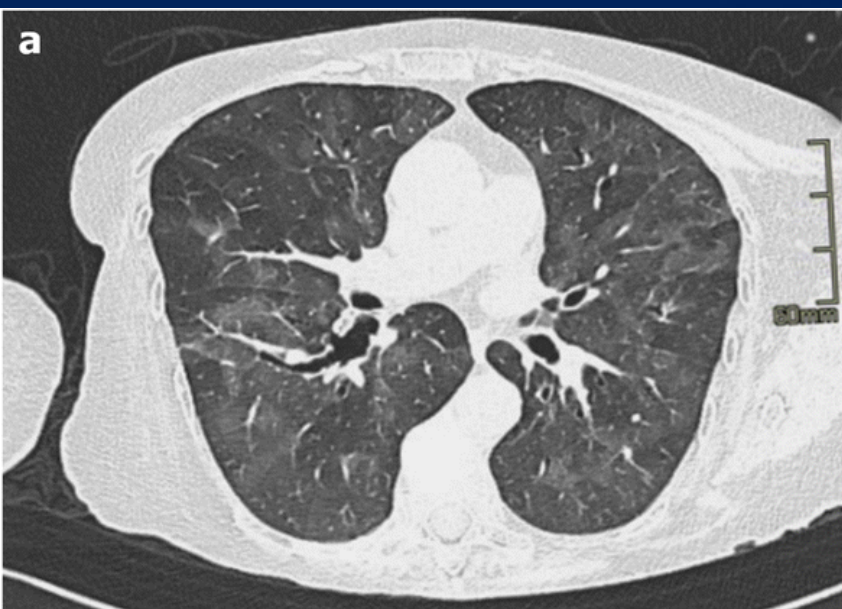




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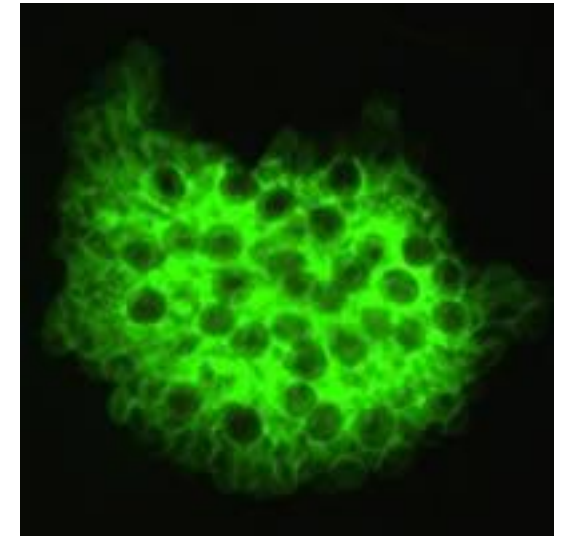




Pneumocystis: Diagnosis

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, calcoflour 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%**



1) Wang Y, et al. Arch Pathol Lab Med. 2007;131(10):1582-4.

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

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

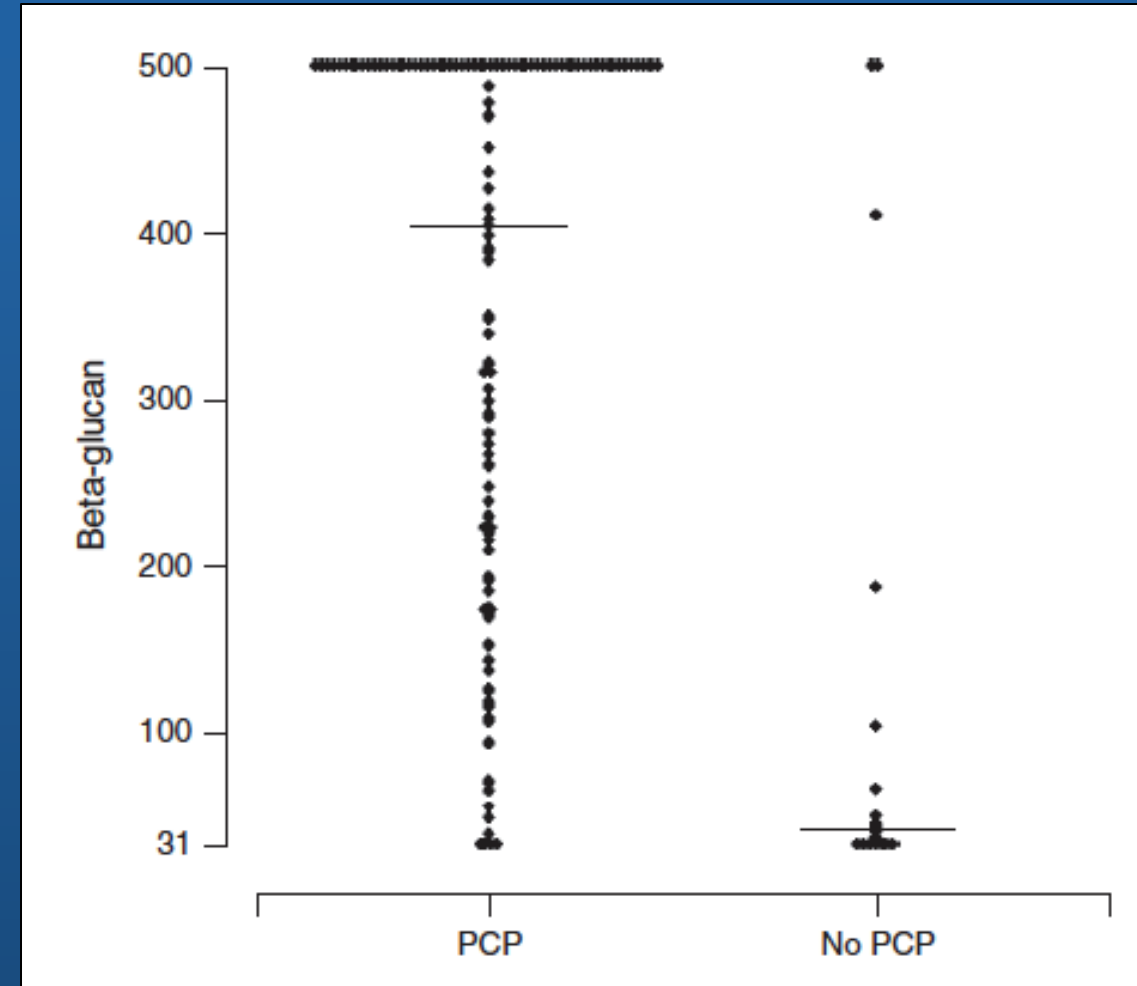
Abbreviations: IFD, invasive fungal diseases; PCP, *Pneumocystis jirovecii* pneumonia; PCR, polymerase chain reaction.

- 1) Bateman M, et al. Med Mycol. 2020;58(8):1015-1028.
- 2) Doyle L et al. OFID. 2017, Sept. doi: 10.1093/ofid/ofx19
- 3) Lagrou K et al. Clin Infect Dis. 2021;72(S2):S114-20.

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)

1-3-Beta-D-Glucan Characteristics	High Pre-Test Probability	Low Pre-Test Probability
Post-test probability of negative result	40%	<u>8%</u>
Post-test probability of positive result	<u>96%</u>	57%



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)

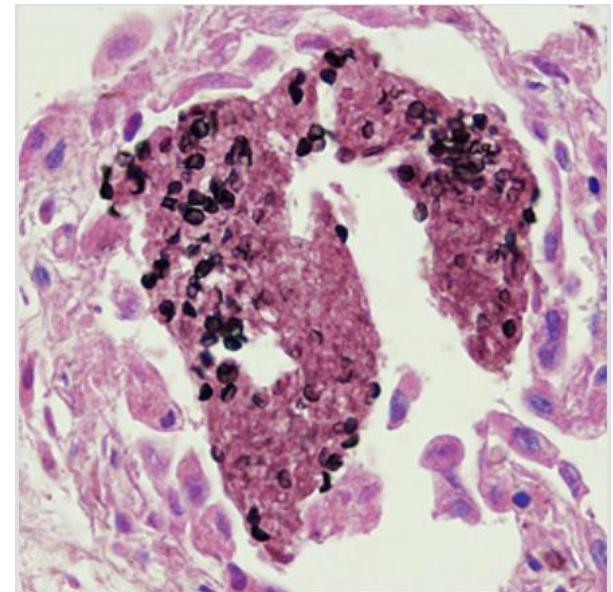


Image of cysts on stain of lung tissue from CDC
(<https://www.cdc.gov/dpdx/pneumocystis/index.html>)

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