Pneumocystis Pneumonia: Part 1

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Disclosures

No conflicts of interest or relationships to disclose.

Pneumocystis Pneumonia: Part 1

- Background & biology
- Clinical manifestations
- Diagnosis

Pneumocystis: Background & Biology

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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

Kovacs JA, Masur H. JAMA. 2009;301(24):2578-2585.

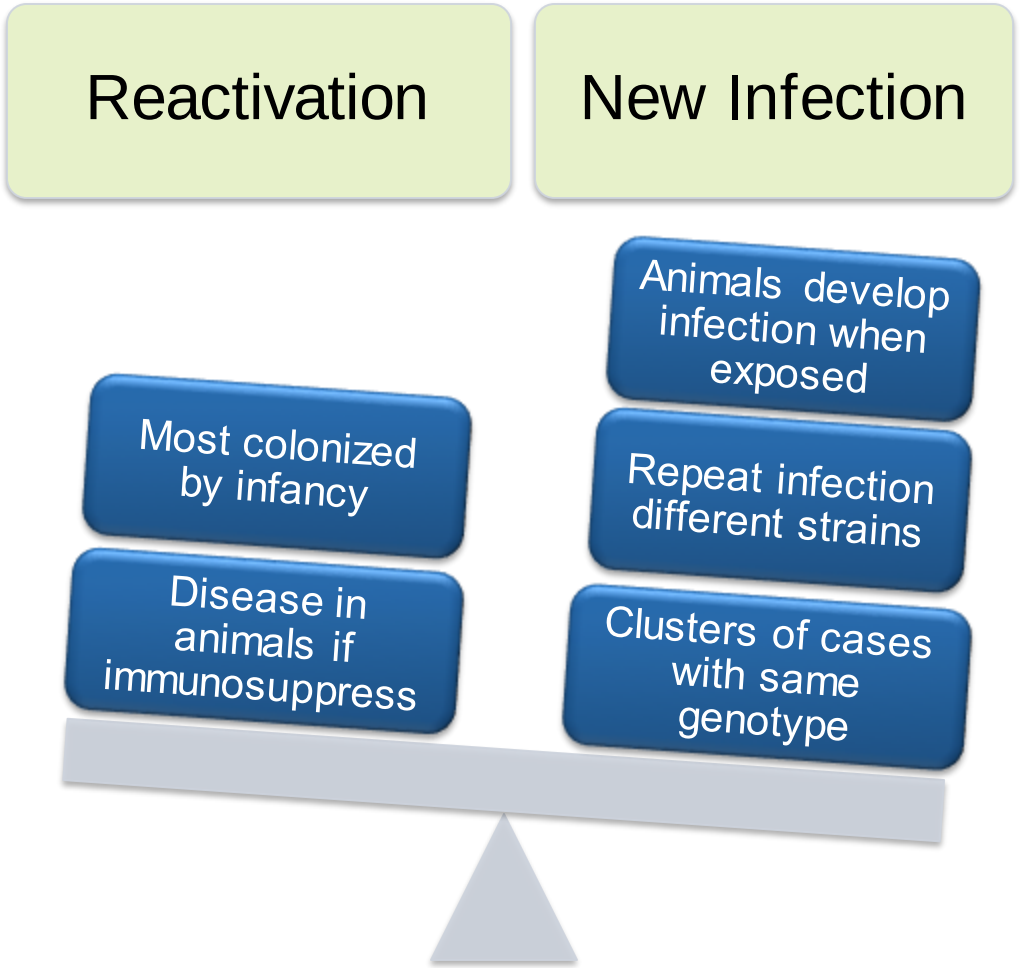
Pneumocystis: Biology

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

Gilroy SA, Bennett NJ. Smin Respir Crit Care Med. 2011;32(6):775-82.
Ma L, Cisse OH, Kovacs JA. Clinical Microbiology Reviews. June 2018.

Pneumocystis Disease: Reactivation vs New Infection



Huang L, et al. Proc Am Thorac Soc. 2011; 8: 294–300

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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.

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Pneumocystis: Clinical Manifestations

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Pneumocystis: Clinical Manifestations

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

Benito N, et al. Eur Resp J. 2012;39:730-745.

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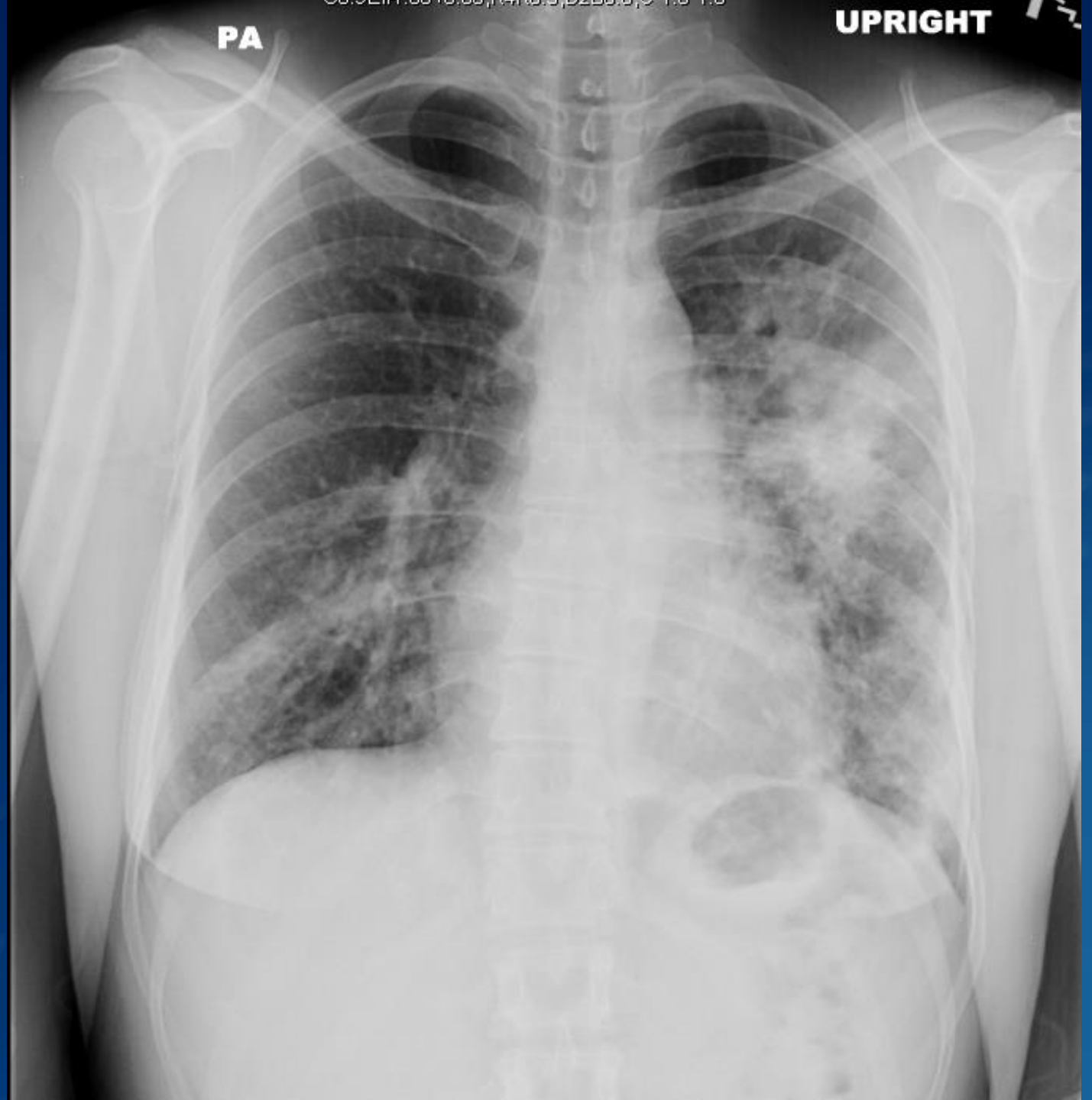

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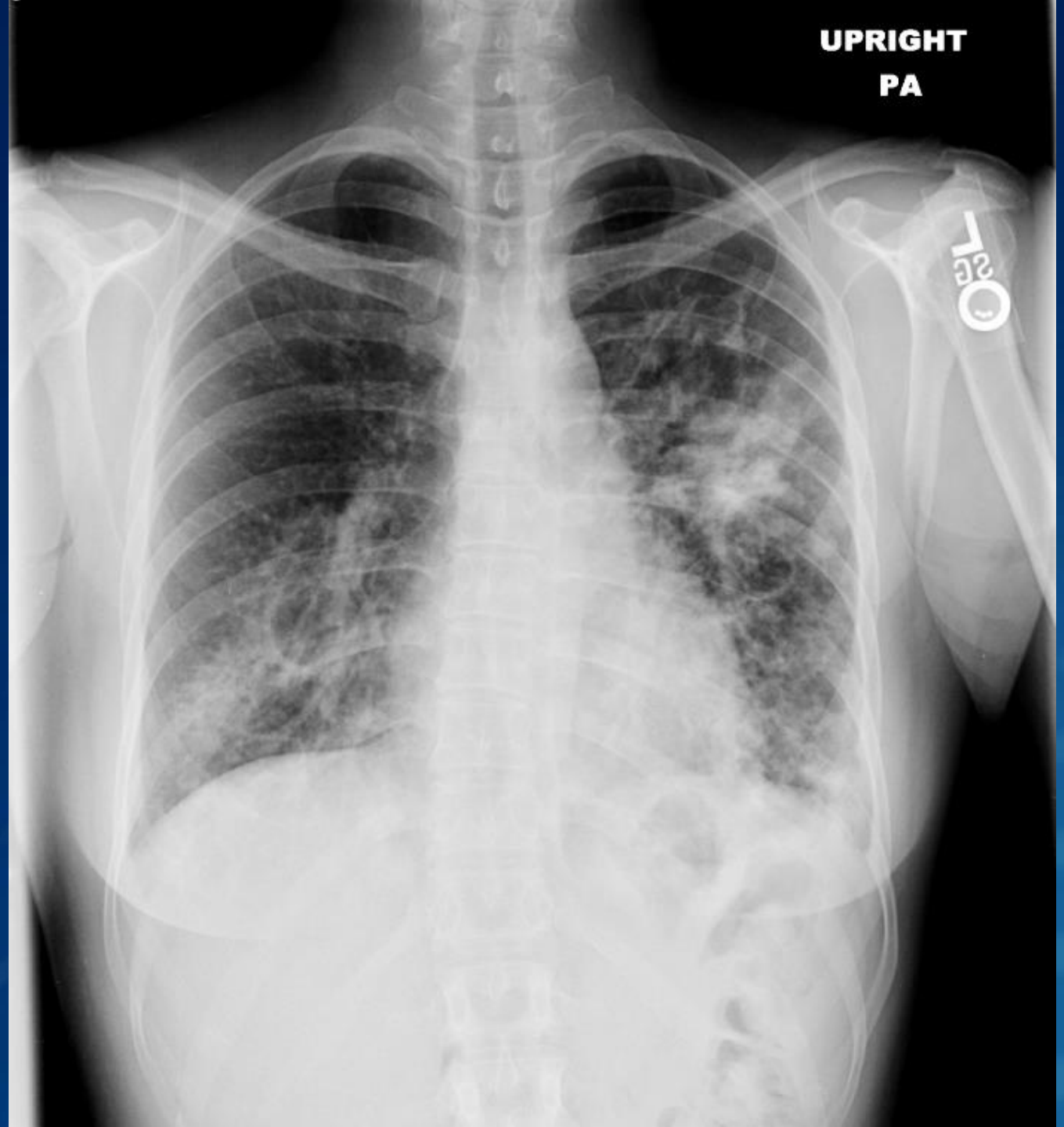
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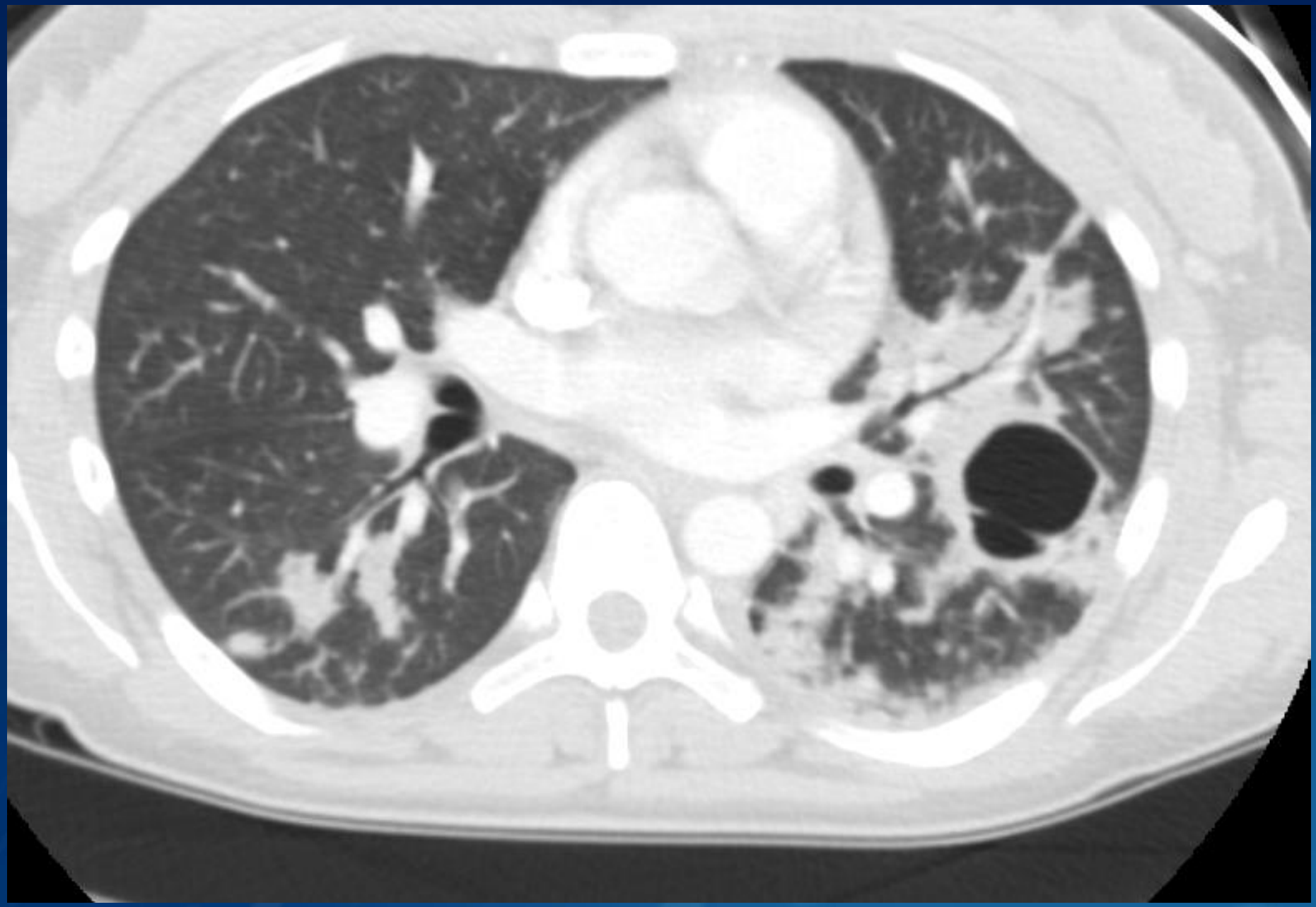

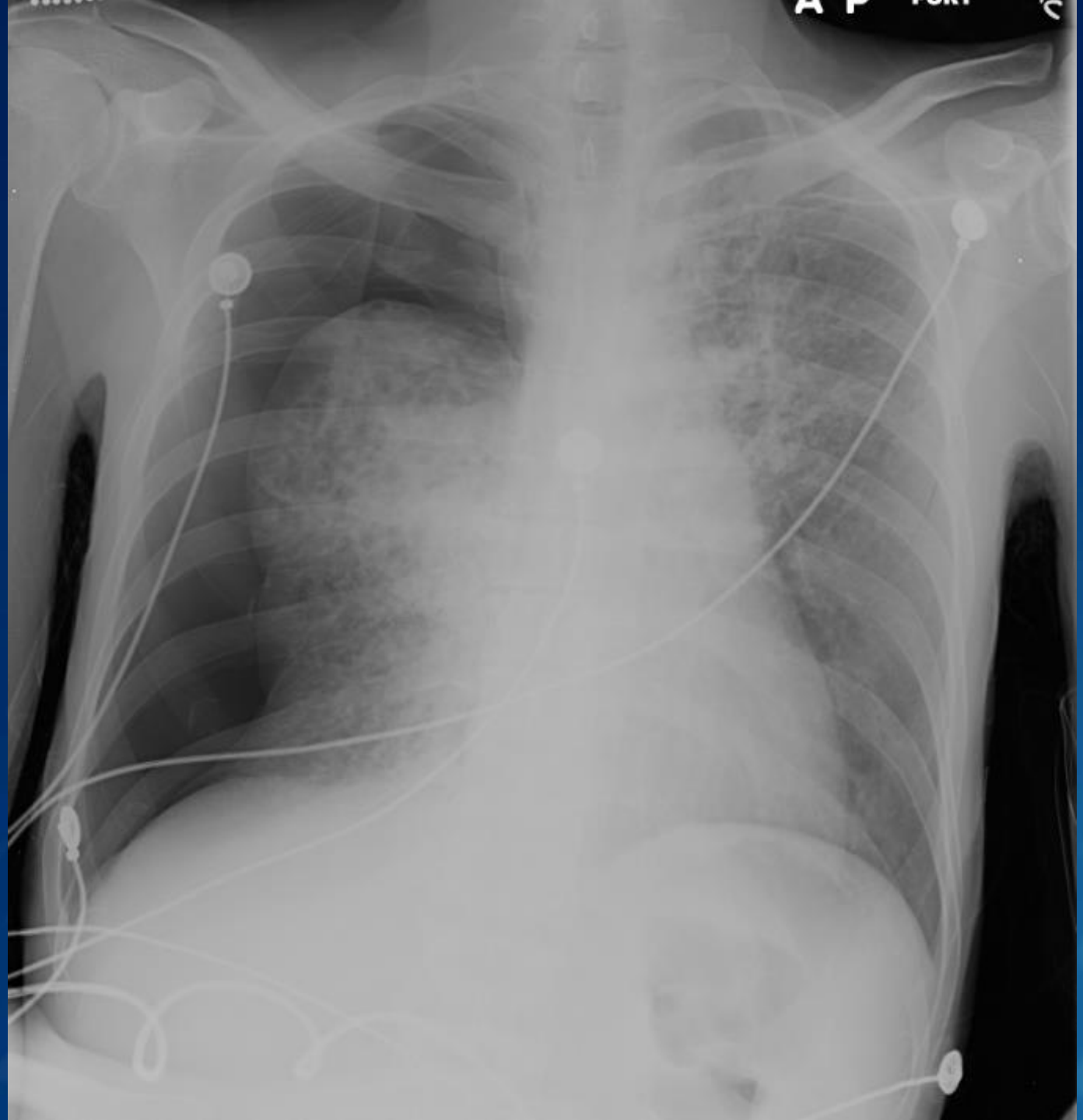
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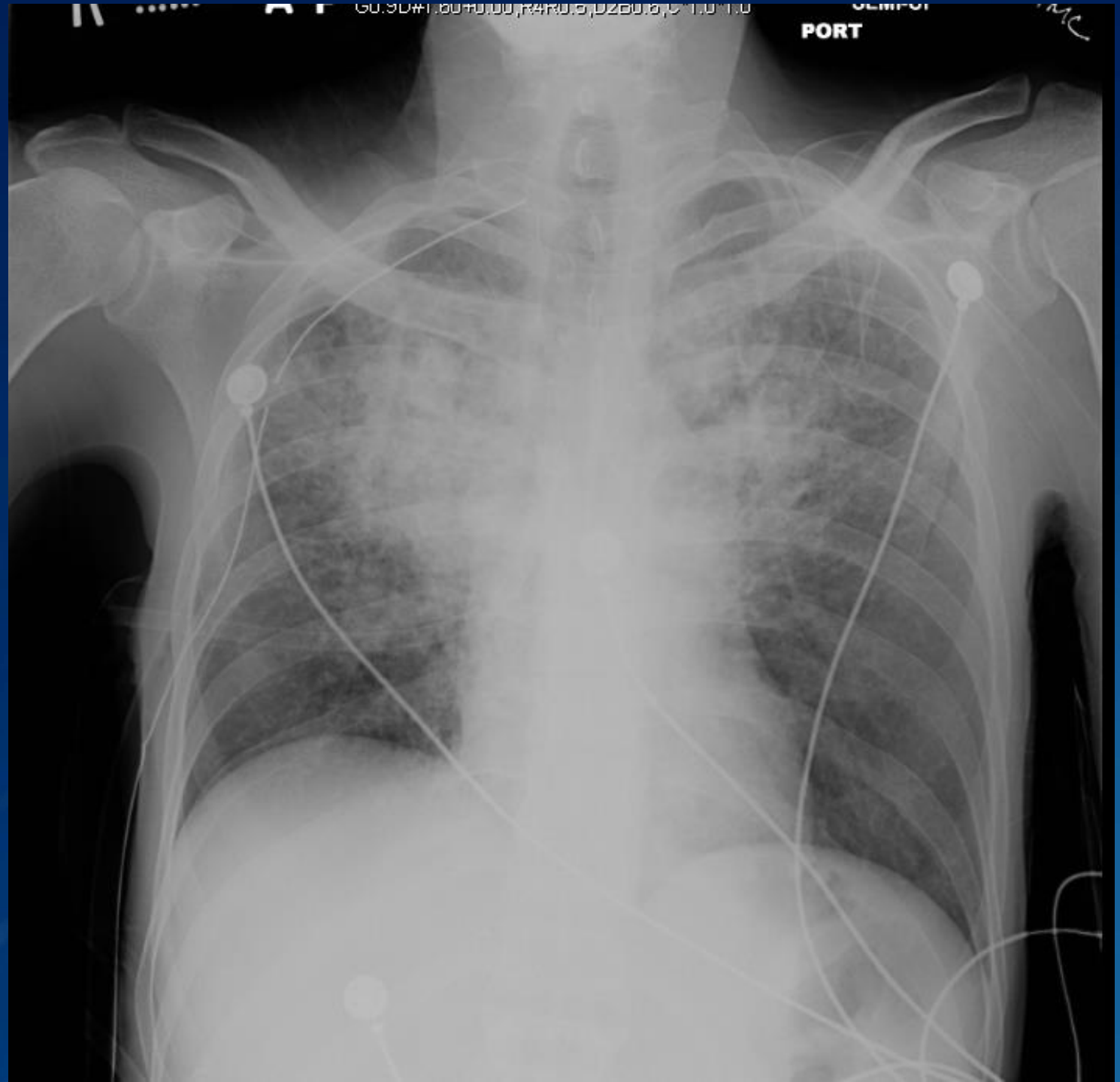
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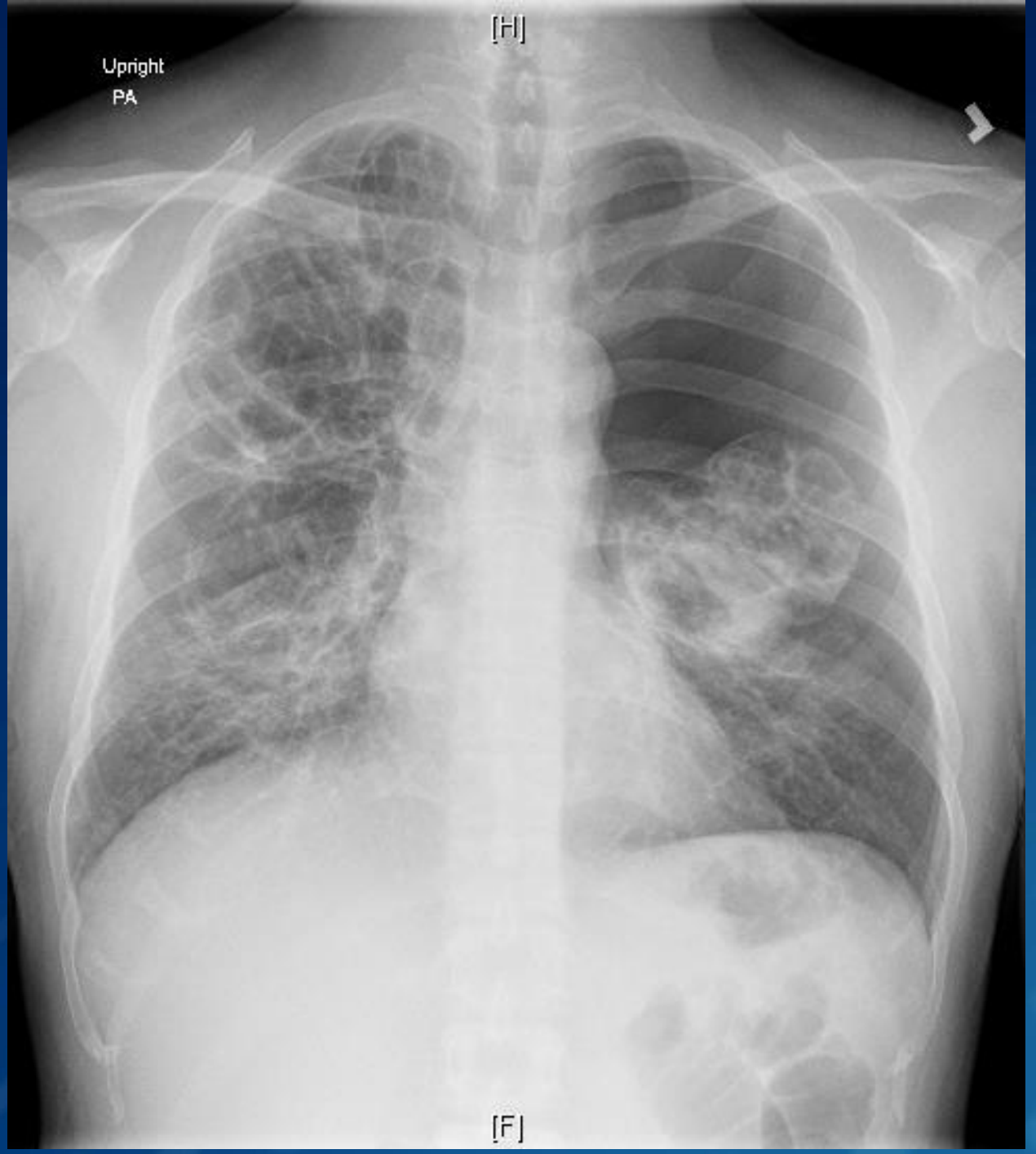
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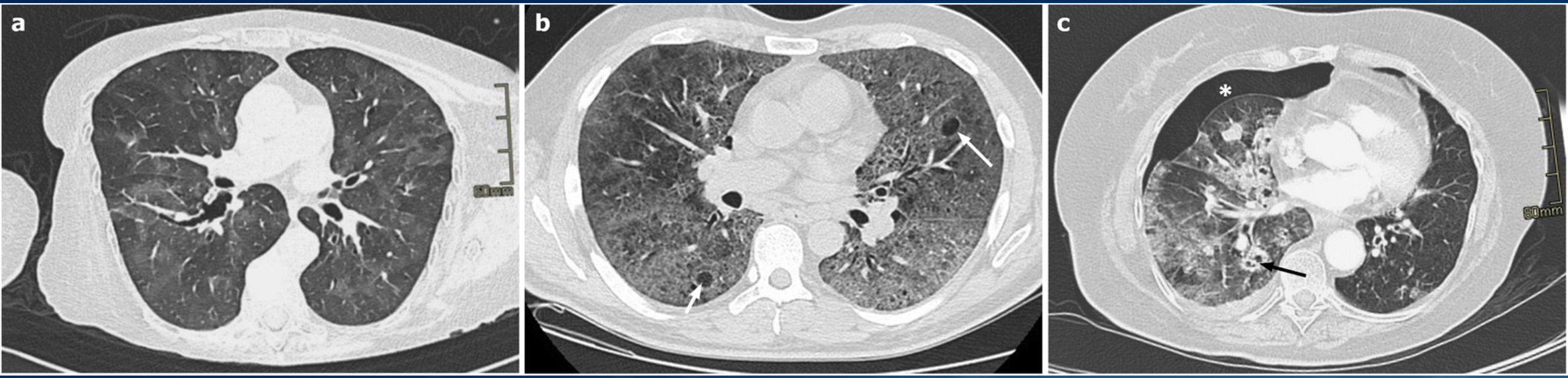
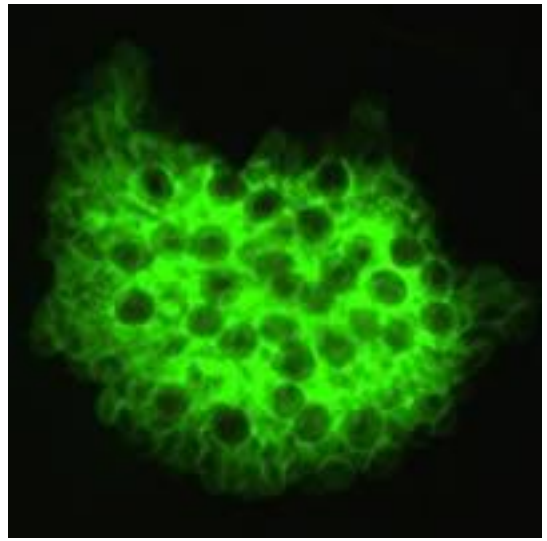


Carlicchi E, et al. Emergency Radiology. 2021;28:507-518.

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)

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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 *P. jirovecii* by microscopy using conventional or immunofluorescence staining in tissue or - Demonstration of *P. jirovecii* by microscopy using conventional or immunofluorescence staining in respiratory specimens
Probable PCP	• Appropriate host factors and clinical and radiologic criteria, plus: - Amplification of *P. jirovecii* 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.

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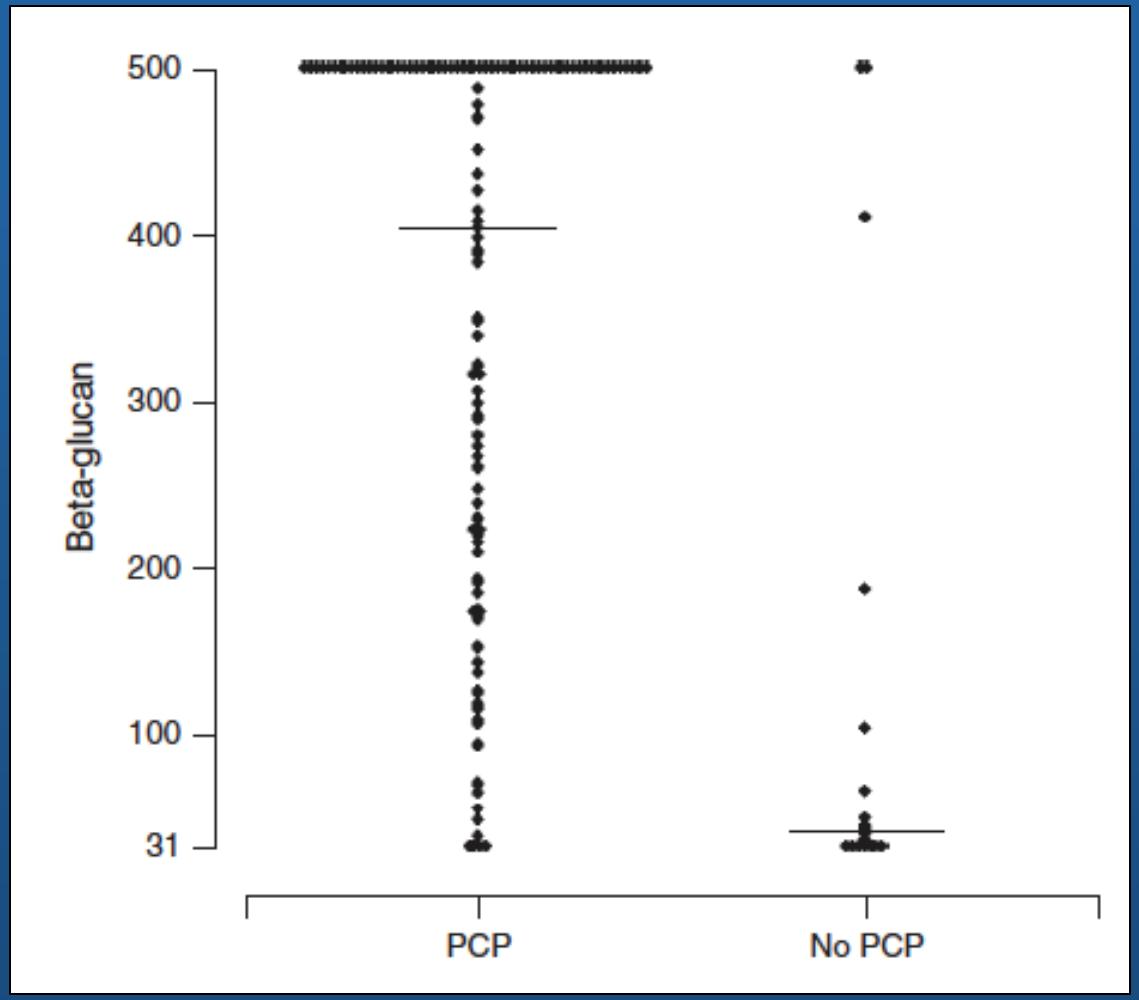
Pneumocystis Diagnosis: Blood Tests

- 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%	8%
Post-test probability of positive result	96%	57%



1) Gilroy SA, Bennett NJ. Semin Respir Crit Care Med 2011;32(6):775-82.
2) Wood BR et al. AIDS. 2013;27(6):967-972. 3) Wood BR et al. AIDS. 2013;27(18):2967-2968.

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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)

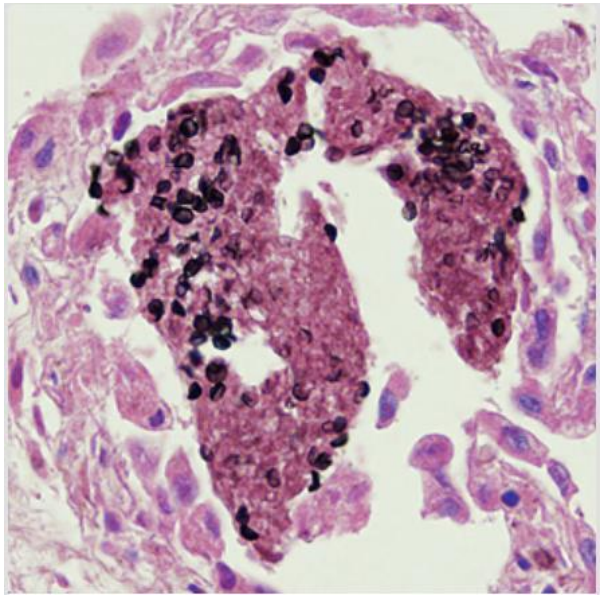

Image of cysts on stain of lung tissue from CDC (https://www.cdc.gov/dpdx/pneumocystis/index.html)

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